AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

NIH IN THE 21ST CENTURY: THE DIRECTOR'S PERSPECTIVE

HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

ONE HUNDRED ELEVENTH CONGRESS

SECOND SESSION

JUNE 15, 2010

Serial No. 111–133

Printed for the use of the Committee on Energy and Commerce

energycommerce.house.gov

U.S. GOVERNMENT PRINTING OFFICE

77–910 WASHINGTON : 2013

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

COMMITTEE ON ENERGY AND COMMERCE

HENRY A. WAXMAN, California, *Chairman*

JOHN D. DINGELL, Michigan
Chairman Emeritus
EDWARD J. MARKEY, Massachusetts
RICK BOUCHER, Virginia
FRANK PALLONE, JR., New Jersey
BART GORDON, Tennessee
BOBBY L. RUSH, Illinois
ANNA G. ESHOO, California
BART STUPAK, Michigan
ELIOT L. ENGEL, New York
GENE GREEN, Texas
DIANA DEGETTE, Colorado
Vice Chairman
LOIS CAPPS, California
MICHAEL F. DOYLE, Pennsylvania
JANE HARMAN, California
TOM ALLEN, Maine
JANICE D. SCHAKOWSKY, Illinois
CHARLES A. GONZALEZ, Texas
JAY INSLEE, Washington
TAMMY BALDWIN, Wisconsin
MIKE ROSS, Arkansas
ANTHONY D. WEINER, New York
JIM MATHESON, Utah
G.K. BUTTERFIELD, North Carolina
CHARLIE MELANCON, Louisiana
JOHN BARROW, Georgia
BARON P. HILL, Indiana
DORIS O. MATSUI, California
DONNA M. CHRISTENSEN, Virgin Islands
KATHY CASTOR, Florida
JOHN P. SARBANES, Maryland
CHRISTOPHER S. MURPHY, Connecticut
ZACHARY T. SPACE, Ohio
JERRY MCNERNEY, California
BETTY SUTTON, Ohio
BRUCE L. BRALEY, Iowa
PETER WELCH, Vermont

JOE BARTON, Texas
Ranking Member
RALPH M. HALL, Texas
FRED UPTON, Michigan
CLIFF STEARNS, Florida
NATHAN DEAL, Georgia
ED WHITFIELD, Kentucky
JOHN SHIMKUS, Illinois
JOHN B. SHADEGG, Arizona
ROY BLUNT, Missouri
STEVE BUYER, Indiana
GEORGE RADANOVICH, California
JOSEPH R. PITTS, Pennsylvania
MARY BONO MACK, California
GREG WALDEN, Oregon
LEE TERRY, Nebraska
MIKE ROGERS, Michigan
SUE WILKINS MYRICK, North Carolina
JOHN SULLIVAN, Oklahoma
TIM MURPHY, Pennsylvania
MICHAEL C. BURGESS, Texas
MARSHA BLACKBURN, Tennessee
PHIL GINGREY, Georgia
STEVE SCALISE, Louisiana

SUBCOMMITTEE ON HEALTH

FRANK PALLONE, JR., New Jersey, *Chairman*

JOHN D. DINGELL, Michigan
BART GORDON, Tennessee
ANNA G. ESHOO, California
ELIOT L. ENGEL, New York
GENE GREEN, Texas
DIANA DEGETTE, Colorado
LOIS CAPPS, California
JANICE D. SCHAKOWSKY, Illinois
TAMMY BALDWIN, Wisconsin
MIKE ROSS, Arkansas
ANTHONY D. WEINER, New York
JIM MATHESON, Utah
JANE HARMAN, California
CHARLES A. GONZALEZ, Texas
JOHN BARROW, Georgia
DONNA M. CHRISTENSEN, Virgin Islands
KATHY CASTOR, Florida
JOHN P. SARBANES, Maryland
CHRISTOPHER S. MURPHY, Connecticut
ZACHARY T. SPACE, Ohio
BETTY SUTTON, Ohio
BRUCE L. BRALEY, Iowa

NATHAN DEAL, Georgia,
Ranking Member
RALPH M. HALL, Texas
BARBARA CUBIN, Wyoming
JOHN B. SHADEGG, Arizona
STEVE BUYER, Indiana
JOSEPH R. PITTS, Pennsylvania
MARY BONO MACK, California
MIKE FERGUSON, New Jersey
MIKE ROGERS, Michigan
SUE WILKINS MYRICK, North Carolina
JOHN SULLIVAN, Oklahoma
TIM MURPHY, Pennsylvania
MICHAEL C. BURGESS, Texas

CONTENTS

NIH IN THE 21ST CENTURY: THE DIRECTOR'S PERSPECTIVE

TUESDAY, JUNE 15, 2010

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 1:11 p.m., in Room 2123 of the Rayburn House Office Building, Hon. Frank Pallone, Jr. [Chairman of the Subcommittee] presiding.

Members present: Representatives Pallone, Dingell, Gordon, Eshoo, Engel, Green, DeGette, Capps, Baldwin, Barrow, Christensen, Castor, Sarbanes, Murphy of Connecticut, Space, Waxman (ex officio), Shimkus, Whitfield, Pitts, Burgess, Blackburn and Gingrey.

Staff present: Bruce Wolpe, Senior Advisor; Ruth Katz, Chief Public Health Counsel; Sarah Despres, Counsel; Robert Clark, Policy Advisor; Stephen Cha, Professional Staff Member; Virgil Miller, Professional Staff Member; Anne Morris, Professional Staff Member; Alvin Banks, Special Assistant; Allison Corr, Special Assistant; Emily Gibbons, Professional Staff Member; Lindsay Vidal, Special Assistant; Earley Green, Chief Clerk; Clay Alspach, Minority Counsel, Health; and Ryan Long, Minority Chief Counsel, Health.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Good morning, or is it afternoon, I should say. We are having a hearing today and we are hearing from just one witness, Dr. Francis Collins, the director of the National Institutes of Health, and I think the members of the Energy and Commerce Committee are of course well acquainted with your great leadership that you have shown at NIH dating back to 1993 when you started your 15-year successful tenure as the director of the National Human Genome Research Institute. Your efforts as director of NHGRI resulted in discovering a number of important genes including those responsible for cystic fibrosis, neurofibromatosis, Huntington's disease, a familial and doctrine cancer syndrome, and most recently, genes for type 2 diabetes. And this work contributed to your being awarded the Presidential Medal of Freedom in 2007 as well as the National Medal of Science in 2009, the highest honor bestowed on scientists by the United States government. So we welcome your well-informed perspective today.

I just wanted to say that the outstanding biomedical research that NIH supports has had a transformative effort on our national health. U.S. life expectancy has dramatically improved over the past century as diseases once fatal have enjoyed scientific discoveries resulting in targeted, effective and personalized treatment strategies. Patients once crushed by no treatment or toxic treatments of nominal value benefit from the collaborative, innovative work done by some of the world's best researchers here in Bethesda and all 50 States and in 90 countries around the world, and I am personally proud of the great partnership the NIH has with Rutgers University in my district as well as with the University of Medicine and Dentistry of New Jersey Medical School, which is the Nation's largest freestanding public health science university.

Now, we commend the progress NIH has made and cheer you on for the discoveries we know you will realize in the future. From Alzheimer's to autism to cancer to heart disease, we know that our federal dollars are hard at work. While I could go on at length about all the research you and your team are undertaking, I just wanted to mention a couple of examples. As you certainly are well aware, the war against cancer continues, and for good reason. Nearly 500,000 people die annually of the disease, but research conducted by NIH has resulted in the overall cancer rate decreasing and treatment is no longer reactive but proactively targeted to the genetic profile of each patient's cancer.

Further, NIH's collaboration with public and private entities strengthens the global effort to fight infectious diseases. Antimicrobial drug resistance, which has been a subject of examination by the Health Subcommittee, is a top priority of NIH's National Institute of Allergy and Infectious Diseases. NIAID has shepherded basic research on resistance as well as facilitated partnerships with industry and nonprofit organizations to develop programs aimed at better controlling antimicrobial drug resistance. And just this week, NIH researchers announced the identification of two previously unknown steps in the spread of malaria in the bloodstream. Progress like this could have a profound effect on our global health, and today malaria kills over 1 million people annually, the majority of whom are young children in sub-Saharan Africa.

I wanted to say the Energy and Commerce Health subcommittee is proud of its long and productive relationship with NIH. We support the cross-cutting collaboration of researchers across disciplines and empower the NIH to continue to promote innovation in the bipartisan NIH Reform Act of 2006. We look forward to hearing an update today on the fully implemented Act including the work realized through the Common Fund.

Dr. Collins, if I could just take a minute, though, before I turn over to our ranking member, Mr. Shimkus. I wanted to take a minute, if I could, from my colleagues' time or, you know, add to our time to thank a long-time member of my staff and the Energy and Commerce Health Subcommittee, Bob Clark or Bobby Clark. I always call him Bob and everybody else calls him Bobby. Would you stand up a minute, Mr. Clark? Most of you know him as being a staff member of the Health Subcommittee but actually he is kind of—I don't know—I guess the best example I have ever had of someone who actually walked into my district office as an intern

at Rutgers University, worked as an intern, then was hired to work on the campaign, then worked as a staff person in the district office for a couple years, and then said he wanted to go to Washington, which I thought was a good idea. He came down to Washington, worked as a legislative person. Were you the receptionist before you even did that? I think he was even the receptionist for a while. And then he became a legislative assistant and then he went to Georgetown and got an M.A. in public health or health. Then he came back and worked as the legislative person on health care, and then finally went to the Health Subcommittee. Now he is moving on again. But I think he is probably—he may have been the only person who did absolutely everything, you know, from being the Rutgers intern all the way now to being on the Health Subcommittee staff. And you can't imagine the things I had him doing, not just health care but Native American and everything else on earth, and he is also obviously a proud alumnus of Rutgers University. So I just wanted to take the time to mention that Bob is leaving at the end of this week and we wish him Godspeed.

I will now yield to Mr. Shimkus, our ranking member. Thank you.

OPENING STATEMENT OF HON. JOHN SHIMKUS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

Mr. SHIMKUS. Thank you, Mr. Chairman.

Let me join you in wishing Bobby Godspeed in his new profession. He now gets to go into the private sector. He may become more Republican because of that, and I look forward to visiting with him real soon.

Thanks for the hearing. It is an important hearing. NIH is something that we all have said for numerous years is an important thing even when I first came here just doubling NIH funding which, you know, happened under Republican stewardship, was a big deal. We never have enough money for basic research and we always ask for more. So we are all very supportive of what can be done. We are particularly excited about, as the ranking member on the Health Subcommittee and even before that, the personal experiences of individuals with diseases of cancers. We are excited in this cancer genome atlas gastric cancer is now going to be included.

Everybody wants more money for every research facility but I do think that in this discussion of cancers if we focus on those that aren't cured right now or can't be delayed in doing the research like on the gastric survival rate, getting people to survive, then we can move in a direction. So I know the committee was gracious in testimony we had earlier this year. That has been followed up by appropriation hearings. For Americans age 25 to 39, one's likelihood of being diagnosed with gastric cancer has increased almost 70 percent since 1977. So it is something, everyone has causes and that is one that we have been working on. So we will focus on that.

I am going to keep my opening comments short. We are concerned about the influx of cash in the stimulus bill and the 2-year focus because most of your stuff goes longer years than that and we are concerned about, well, what went well and what went poorly and because of the limited time frame.

I can't leave a health care hearing without talking about the new health care law. We were told it would save average premiums $2,500 a year. CBO says it is going to increase premiums $2,000 a year. But next week the new temporary high-risk pool program should go online, and informal discussions with some States, these high-risk pools are going to have to do something we said we weren't going to do. They are going to have to cap enrollees. They are going to have to create preexisting condition exclusion. Those are things we could fix if we would just talk about this new law and try to address some of the reforms.

So not as long as I normally go, Mr. Chairman. Thank you for your time and I yield back.

[The prepared statement of Mr. Shimkus follows:]

STATEMENT OF RANKING MEMBER JOHN SHIMKUS

JUNE 15, 2010 Hearing – "NIH in the 21st Century: The Director's Perspective"

Mr. Chairman, thank you for holding this hearing on the National Institutes of Health's research activities and priorities.

I'd like to welcome Dr. Collins, who is the Director of the National Institutes of Health. We look forward to hearing your testimony.

NIH is the Federal government's principal medical research agency.

NIH's mission is to advance research in pursuit of fundamental knowledge that will lead to better health outcomes.

In my years in Congress, I've been a strong supporter of the National Institutes of Health.

This week I co-wrote a letter with Senator Durbin to the National Cancer Institute of the National Institutes of Health, expressing our support for federal investment by the National Cancer Institute (NCI) to find a cure for gastric cancer.

As you know, gastric cancer is one of the deadliest cancers in the U.S.

In 2009, there were an estimated 10,620 deaths from gastric cancer.

The five year survival rate for metastatic gastric cancer is 3.4 percent, one of the five lowest cancer survival rates.

This lethal cancer is increasing exponentially in young people. Just last month, the National Cancer Institute released a study based on surveillance tracking of gastric cancer. The study demonstrated the dramatic increase in gastric cancer in young people. For Americans age 25-39, one's likelihood of being diagnosed with gastric cancer has increased dramatically by almost 70 percent since 1977.

In addition to allowing us to learn more about the research activities of NIH, this hearing provides an opportunity for the Subcommittee to provide oversight of the NIH's implementation of the NIH Reform Act of 2006 and the Obama-Pelosi $787 "Stimulus" bill.

Back in 2006, the members of this Committee led Congress in enacting the NIH Reform Act.

The goal of the NIH Reform Act was to improve NIH's overall performance and increase the opportunities for research activities for all health conditions.

I look forward to hearing how NIH has implemented the Reform Act.

There are currently 27 Institutes and Centers at the NIH that focus on certain areas of the bodies or specific conditions. Prior to the NIH Reform Act, the Institutes seemed to function in isolation even though diseases rarely do. The Reform Act created the Common Fund designed to fund cross-institute research which will facilitate multi-institute projects of great promise.

The law also created the "Scientific Management Review Board" charged with formally and publicly reviewing NIH's organizational structure at least once every seven years. I look forward to hearing from Dr. Collins on the creation and work of the Management Review Board.

Last year, Congress enacted the $787 "Stimulus Bill" chalk full of wasteful spending and unfulfilled promises.

The Stimulus Bill did not create jobs. Before the Stimulus passed, Obama Administration officials predicted that passing the Stimulus would keep the unemployment rate under 8 percent, while failing to pass the Stimulus could send unemployment over 9 percent. As we all know, the unemployment rate stands just below 10 percent, and the only jobs being created in this country are temporary Census worker jobs.

To make matters worse, the Stimulus added even more debt than Congress expected as recent cost estimates of the Stimulus have risen to $862 billion, adding billions more to our national debt.

The Stimulus Bill included $10 billion for NIH. However, there is substantial concern that the $10 billion for NIH is not being used effectively.

The NIH's function is to further scientific and medical understanding and research; its mission is not job creation.

Typically, an individual receiving an NIH grant will receive funds over a four to five year cycle. The type of research conducted by NIH grantees is time intensive. Clinical trials and other scientific endeavors take time to develop, conduct, and then analyze.

Unfortunately, the NIH Stimulus money is not being used to fund these time intensive grants. Instead, the money must be used on two year grants. This two year limitation on NIH Stimulus grants will lead to little in terms of advanced scientific or medical understanding.

I'm glad we are doing oversight of the NIH Reform Act and Stimulus bill today. Mr. Chairman, it is clear to everyone that we need to extend this oversight to the new health law.

The bad news just keeps pouring in, but this Congress wants to ignore the fact that we just passed trillion dollar legislation that will affect every person in America.

The missed deadlines are piling up yet the Administration is wasting its time sending out propaganda.

The proponents of the law promised Americans that they could keep their current health insurance if they like it. Now, the Administration is preparing regulations that could force at least 51% of employers to have to change their health plans. In fact, that number could be as high as 69%.

Americans were told that their health care premiums would be reduced by an average of $2,500 a year. However, the Congressional Budget Office has reported that Americans' premiums will actually increase by over $2,000 a year.

Next week, the new, temporary high risk pool program should go online. However, many questions remain about its operation, and this Committee has done nothing to try to answer them.

1. Will people really have to be uninsured for six months before receiving coverage?
2. Will those states that currently have a high risk pool be required to create a whole new program in order to contract with HHS?
3. Finally, will the design of the program encourage irresponsible states to spend their allotments quickly while responsible states have their funds raided? These are questions for a program that starts NEXT WEEK.

When a 3,000 page bill refers to the Secretary of HHS over 2,000 times, Congress has the responsibility to monitor the unlimited discretion that we have provided these bureaucrats.

I yield back the balance of my time.

Mr. PALLONE. Thank you, Mr. Shimkus.

I yield to our chairman of the full committee, Mr. Waxman.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you very much, Chairman Pallone. I thank you for this hearing. And I also want to pay tribute to Bobby Clark. While he was part of your subcommittee staff, he was part of the team working tirelessly on health reform. He was famous among the staff for his amazing command of detail and his calm-in-the-storm demeanor, and we will miss him and we all wish him well in his new endeavor.

For the hearing today, it is a great pleasure to have the new director of the NIH, Dr. Francis Collins, come and testify. He is a renowned researcher who among other scientific achievements led the government's effort to map the human genome. NIH is the preeminent health research institution in the world. It is recognized across the country and around the globe its outstanding work, and with good reason. The research NIH supports and conducts not only has resulted in cutting-edge scientific breakthroughs, it also led to real and meaningful improvements in public health.

But the work of NIH truly is never done. Even, as we learn more about disease and the human condition, the list of research challenges grows. Some 40 years ago, for example, we thought of cancer as a single disease and now—it is much more complicated. Because of its outstanding work, we continue to look to NIH to help solve the trickiest of medical riddles such as Alzheimer's disease, diabetes, autism, spinal cord injury, Parkinson's disease and many others, and we also look to NIH to figure out how to prevent disease and disability wherever we can. Our job in the Congress is to ensure that NIH has the funding it needs for its researchers to continue their world-class work. Money is in short supply, I know, but federal support for NIH is not where we can afford to cut back.

In this time of both endless research possibilities, basic and translational, and difficult economic challenges, Dr. Collins has come forward to lead NIH and the brilliant researchers it supports. We are eager to hear from him about his plans and how best in the years ahead to meet NIH's mandate and continue the institute's longstanding legacy for making an immeasurable difference in the lives of all Americans. Thank you very much, Dr. Collins, for being here and to share your plans and priorities at NIH with us.

Yield back the balance of my time.

[The prepared statement of Mr. Waxman follows:]

Statement of Chairman Henry A. Waxman
Committee on Energy and Commerce
Subcommittee on Health Hearing
"NIH in the 21st Century: The Director's Perspective"
June 15, 2010

Today, we have the great pleasure of hearing from the new Director of the National Institutes of Health, Dr. Francis Collins. In addition to his responsibilities as head of NIH, Dr. Collins is a renowned researcher who, among many other scientific achievements, led the government's effort to map the human genome.

I want to thank Chairman Pallone for convening this important hearing.

NIH is **the** preeminent health research institution in the world.

It is recognized across the country and around the globe for its outstanding work.

And with good reason. The research NIH supports and conducts not only has resulted in cutting edge scientific breakthroughs; it has also led to real and meaningful improvements in the public's health.

From work on breast, cervical and prostate cancer to Hepatitis B; from hypertension to the H1N1virus; from HIV/AIDS to sudden infant death syndrome-- to name just a few of our most pressing medical concerns -- NIH researchers have made discoveries, developed treatments, and even found cures that have allowed us to live longer, healthier, and more productive lives.

But the work of NIH truly is never done. Indeed, as we learn more about disease and the human condition, the list of research challenges grows exponentially. Some 40 years ago, for example, we thought a single, targeted war on cancer was all that was needed to wipe out that illness.

Today, of course, through the efforts of NIH and others, we understand that cancer -- in all of its many forms -- is a far more complicated disease – that it is, in fact, a series of diseases. Thus, the NIH portfolio of cancer research has grown significantly, and become more complex.

Because of its outstanding work, we continue to look to NIH to help solve the trickiest of medical riddles such as Alzheimer's disease, diabetes, autism, spinal cord injury, Parkinson's disease, among others.

We must look to NIH as well to figure out how to prevent disease and disability wherever we can.

Meeting these expectations demands nothing less than the best researchers, exceptional grant applications, strong leadership, and sustained funding.

We know that NIH is populated with great researchers – individuals with the finest scientific minds who increasingly are collaborating across disciplines and generating innovative proposals with a real "bench-to-bedside" approach to research.

We also appreciate that NIH has long and robust relationships with the country's top research institutions and many of the scientists employed by them. These are the people who make NIH the premier research organization that it is.

Our job -- the job of Congress -- is to ensure that NIH has the funding it needs for its researchers to continue their world-class work. Money is in short supply, I know, but federal support for NIH is not where we can afford to cut back.

In this time of both endless research possibilities -- basic and translational -- and difficult economic challenges, Dr. Collins has come forward to lead NIH and the brilliant researchers it supports.

We are eager to hear from him about his plans for NIH in the 21st century: how best, in the years ahead, to meet NIH's mandate and continue the Institutes' long-standing legacy for making an immeasurable difference in the lives of all Americans.

Dr. Collins, thank you so much for coming to share your plans and priorities for NIH with us today. I look forward to hearing your testimony.

Mr. PALLONE. Thank you, Chairman Waxman.

Next is the gentleman from Texas, Mr. Burgess.

Mr. BURGESS. Thank you, Mr. Chairman.

Welcome, Dr. Collins, to our humble little committee.

I am going to submit my statement for the record and reserve time for questions because we rarely get a witness with this much firepower, and time is better spent for questions, so I will yield back.

[The information was unavailable at the time of printing.]

Mr. PALLONE. Thank you.

Our chairman emeritus, Mr. Dingell.

Mr. DINGELL. Thank you, Mr. Chairman. I commend you for this hearing. I look forward to the result of it, and I ask to revise and extend my remarks. I have an admirable statement which everyone will enjoy reading.

[The prepared statement of Mr. Dingell follows:]

Statement of
the Honorable John D. Dingell

Subcommittee on Health Hearing
"NIH in the 21st Century: The Director's Perspective"

June 15, 2010

Thank you, Mr. Chairman.

The National Institutes of Health (NIH) is the premier medical research agency of the federal government. The work coordinated by its leadership, and carried out by its researchers, both intramural and extramural, is responsible for many important discoveries that have improved the health and saved the lives of our citizens.

Much progress has been made in advancing what we know about, and how we respond to, the complex health conditions of the day, including cardiovascular disease, cancer, Alzheimer's disease, diabetes, and obesity. However, much remains to be done. We are finding that the diseases confronting our people are more complex. As a result, our understanding of these diseases must be more detailed and the things we learn must be translated in meaningful ways.

NIH has seen an increase in its funding over the past few years. The additional funding has fostered new, innovative approaches at the Agency, including the acceleration of translational research, better coordination between biomedical research planning and the regulatory review process for new therapies, and a greater focus on rare and neglected diseases.

In addition to the important health advances, NIH research funding is an economic stimulator. NIH conducts and supports outstanding biomedical and behavioral research, through more than 3,000 institutions across the country—institutions that have a direct impact upon the local economies in their towns, cities, and states.

I, and other Members of this Committee, have worked very hard to insulate NIH from the politics associated with their work. Every disease has its own constituency and is worthy of the research attention of NIH. However, it is important that the priorities of the agency and the work done by NIH-funded researchers are based on thoughtful scientific judgment and reflect the complex scientific considerations of the day. It is equally important that the agency's work is carried out in a fair and transparent manner.

Finally, the 2006 NIH reauthorization strengthened the role of the Director and allowed more flexibility for coordination across the Institutes and Centers. I appreciate the opportunity to hear about the Agency's progress since the enactment of the 2006 reauthorization and the other work being undertaken.

I would like to welcome our witness, Dr. Frances Collins, the NIH Director. I would like to thank him for the many valued contributions he has made to this Committee, the Congress, and the advancement of science throughout the years. I still remember his time at the University of Michigan prior to his first stint at NIH in the early 1990's.

Thank you again, Mr. Chairman. I yield back the balance of my time.

Mr. PALLONE. Without objection, so ordered, and any member may submit a statement and we will make it part of the record. Thank you, Chairman.

Next is the gentleman from Georgia, Mr. Gingrey.

OPENING STATEMENT OF HON. PHIL GINGREY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF GEORGIA

Mr. GINGREY. Mr. Chairman, thank you.

The United States is a global leader in medical research and innovation, and we in large part have the National Institutes of Health to thank for these efforts. Today, roughly 30 percent of the funding for disease research equaling almost 3 percent of our gross domestic product comes from the NIH and our federal government. These investments have advanced our understanding and treatment of many life-threatening diseases. Recently, an NIH-funded organization at the University of Illinois-Chicago made national news when they reported finding key genomic markers common in autistic children. These findings may one day support our effort to understand what factors contribute to this disease.

Additionally, a dozen competing drug companies announced late last week that they would be taking the unusual step of sharing data on Alzheimer's disease. The hope is that this database of information created in consultation with NIH will spark news ideas for treatment of that grave disease. I would like to commend you, Dr. Collins, for helping to foster this groundbreaking collaborative approach.

In addition to these efforts, NIH grants have resulted in the discovery and development of many lifesaving medical treatments. Since coming on the market, the combination of the drug Herceptin with chemotherapy has been shown to increase both survival and response rates for patients with breast cancer including reducing the risk of relapse by 50 percent when given to patients immediately following surgery. However, I do want to strike one note of caution. The drug Herceptin is widely available in the United States, but this was not always the case in Britain. England initially denied coverage of the drug and only relented after many public demonstrations including a protest march by thousands of women through the streets of London.

I raise these points because, as many of you know, Dr. Donald Berwick was recently nominated director of the Centers for Medicare and Medicaid Services by President Obama. This is the same Donald Berwick who just last year stated, and I quote, that "the decision is not whether we will ration care. The decision is whether we will ration with our eyes open." To be frank, I fear that the groundbreaking treatments funded by NIH that we are celebrating here today will not be made available to our seniors if the political philosophies of Dr. Berwick are in charge of our Medicare program. Mr. Chairman, our seniors cannot afford that, that kind of support of health care rationing.

I look forward, Dr. Collins, to hearing from you. We are honored with your presence.

Mr. Chairman, with that, I yield back my time.

Mr. PALLONE. Thank you, Mr. Gingrey.

Next is the vice chair of our full committee, the gentlewoman from Colorado, Ms. DeGette.

Ms. DEGETTE. Thank you, Mr. Chairman. I too will submit my statement to the record in order to have more time to ask the wide range of questions I have for Dr. Collins. We are glad to have him here.

[The information was unavailable at the time of printing.]

Mr. PALLONE. Thank you, and as I said, all members' statements will be submitted for the record.

Next is the gentlewoman from Tennessee, Ms. Blackburn.

OPENING STATEMENT OF HON. MARSHA BLACKBURN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Mrs. BLACKBURN. Thank you, Mr. Chairman. Thank you for the hearing, and I want to thank our witnesses for taking the time to be with us.

I will have to tell you that I am one of those that really enjoys watching the research that is taking place in my State of Tennessee. We have over 1,000 NIH research awards totaling over $440 million that were granted in 2009 alone. Tennessee organizations such as Meharry Medical, Vanderbilt University, St. Jude's Children's Hospital as well as several small privately held companies are making advances in the medical field that will improve the lives of everyone. Through the use of NIH funding, the Vanderbilt Institute for Clinical and Translational Research has pioneered many biomedical research advances including important discoveries regarding autism, diabetes and ADHD. Also, with the NIH funding, Vanderbilt Ingram Cancer Center is the only NCI-designated comprehensive cancer center in Tennessee that conducts basic translational and clinical research. Likewise, St. Jude's Children's Hospital in Memphis is using grant money from NIH to lead the way in cancer research and I think we have all noted that St. Jude's was recently named the best children's cancer hospital in the Nation by U.S. News and World Report.

In addition to funding large research institutions, these NIH grants to small privately owned businesses throughout Tennessee such as Max Mobility, which is a small business of less than 10 employees located in Antioch, Tennessee, are producing great results. Max Mobility has used NIH funds to create innovative wheelchair designs and products to greatly assist regular wheelchair users and it is clear that research grants from NIH provide the opportunities for organizations to make and continue these discoveries.

In 2006, this committee passed the NIH Reform Act to cut bureaucracy, increase transparency and streamline interagency communication in order to increase efficiency and to hopefully decrease waste in the funding process. My hope is that we are going to continue on that path. My concern is that with the recent changes in the Administration and the passage of the health care bill that we are going to see a change in those matters.

So I am looking forward to the hearing today, and I yield back my time.

Mr. PALLONE. Thank you.

The gentleman from Connecticut, Mr. Murphy.

OPENING STATEMENT OF HON. CHRISTOPHER S. MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Mr. MURPHY OF CONNECTICUT. Thank you very much, Mr. Chairman. Welcome, Dr. Collins. In discussions beforehand, we realized that Dr. Collins spent some time in my hometown of Cheshire, Connecticut, and his kids actually went to the elementary school in our local neighborhood so it is good to see that it is a small world.

Dr. Collins, in Connecticut we have been wildly successful in the last 4 to 5 years investing in stem cell research lines. Due to federal restrictions, we passed the Nation's first law putting State funds into our two main research institutions of Yale and U. Conn. Yale has been able to leverage about twice as much in private investment money as public investment money due to these funds, and we are right now opening on the U. Conn campus an incubation center for spin-offs from the 40-some stem cell labs that we have at U. Conn today to move into private sector commercialized developments. It is very exciting but it presents our State, sort of new to the area of scientific investment, with some very interesting questions about how to match public and private partnerships and how to make sure that our State investment in some of the basic stem cell research ends up with us sharing in some of the monetary gain to be happened through the commercialization of some of those partnerships.

And so whether it is in your testimony or in some of the questioning, one of the things that I am eager to hear about is how NIH continues to evolve in its thinking about how the scientific research that you fund when it becomes commercialized accrues to the benefit of the taxpayers that have made those investments. I know you are not a biotech venture capital firm. You are in this for the science of it and the lifesaving research, but I hope that we are constantly thinking as we are in Connecticut of new ways to protect taxpayer investments when it leads to a private sector solution that can reap large rewards to a private company even though it is based in part on federally funded research. We are thrilled that you are here. We are very eager to hear your testimony about the new and exciting things happening at NIH so we can bring your stories back to our constituents, and I appreciate the chance to ask some questions later on.

Mr. PALLONE. Thank you, Mr. Murphy.

The gentlewoman from the Virgin Islands, Ms. Christensen.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman.

Although my opening statement is not as brilliant as our chair emeritus, I am going to submit it for the record, and I would like to welcome Dr. Collins.

[The information was unavailable at the time of printing.]

Mr. PALLONE. Thank you.

The gentlewoman from Florida, Ms. Castor.

OPENING STATEMENT OF HON. KATHY CASTOR, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Ms. CASTOR. Thank you very much, Mr. Chairman, for calling the hearing, and welcome, Dr. Collins.

I think medical research in America today is very exciting, and the potential for continued breakthroughs and advances, the potential is unlimited, and in my hometown of Tampa where I represent a large research university, the University of South Florida, that is collocated with a premier cancer research institute in the Moffett Cancer Center.

All of these NIH awards are terrific. The grants are great, it improves the public health, but they are important for our workforce as well as we try to find our way out of economic recovery. What it means to our workforce needs and the potential for young people to have good-paying jobs in a profession that has a great future just cannot be understated.

So I am very interested in your testimony today about the future of NIH, how we can improve all the grant making that you do and provide young people with opportunities in this field and all the great opportunities that lie therein. Thank you very much.

Mr. PALLONE. Thank you.

The gentlewoman from Wisconsin, Ms. Baldwin.

OPENING STATEMENT OF HON. TAMMY BALDWIN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF WISCONSIN

Ms. BALDWIN. Thank you, Mr. Chairman. I appreciate the fact that you are holding this hearing today, and Dr. Collins, I am very grateful that you are here today to share information about the vital role of the National Institutes of Health in our health care system and in our economy.

The NIH is especially important to my hometown of Madison, Wisconsin. It is the largest and most critical source of research funds for the University of Wisconsin-Madison which in my own unbiased opinion is one of the word's premier research institutions.

Basic and applied medical research has and will continue to have a significant impact on the health of Wisconsin's residents and the State's economic growth. Biomedical research has helped raise the average life expectancy of Wisconsin residents from 52 years in 1920 to 79 years in 2005, and every year Wisconsin citizens save an estimated $1.6 billion in health care costs, thanks to public investments in biomedical research and development. And finally, Wisconsin researchers bring in a greater percentage of federal bioscience funding per capita than any other federal program or expenditure in the State generating thousands of high-quality, high-paying jobs for our residents.

And I want to add just a little personal note. As somebody who was raised by her grandparents and having one grandparent who was a biochemist, I was certainly personally raised off NIH funds, so I have a personal debt of gratitude to the NIH and the grants. NIH grants have trained students and created jobs. They have fostered significant scientific progress and saved lives.

Yet certainly challenges lie ahead. Budget constraints and limited funding for infrastructure improvements restrict the capacity

of research institutions to take biomedical research to the next level, and we must nurture young researchers and ensure that the next generation of scientists stays in the field.

So I look forward to your testimony, Dr. Collins, and thank you for being here today, and Mr. Chairman, I yield back the remainder of my time.

Mr. PALLONE. Thank you.

Next is our subcommittee vice chair, Ms. Capps.

OPENING STATEMENT OF HON. LOIS CAPPS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mrs. CAPPS. Thank you, Chairman Pallone, for inviting Dr. Collins to testify before us today, and thank you, Dr. Collins, for joining us here. I have been waiting for this occasion, and I will take less than a minute just to say this is really about us listening to you, about the fascinating work being done at the Institutes now, the direction you would like to take the Institutes into the future and how Congress can best legislate the authorities for you to meet your goals which are our goals as well.

Most importantly, how can we keep up with the pace and the direction of scientific discovery? How can we move to more quickly translate those discoveries into practice, both in treatment and in prevention? I bring up prevention because so often we think about basic research that leads to the development of chemical drugs, biologics, medical devices, but there are also very many opportunities to nip disease in the bud, to diagnose more efficiently and more quickly, and to prevent diseases before they ever develop.

So I look forward to hearing from you. Thank you very much.

Mr. PALLONE. Thank you. I think we have had every member of the subcommittee do an opening statement so we will move to you, Dr. Collins. And let me say to the members that Dr. Collins had asked to speak longer than usual. I don't know if it was 12 or 15 minutes, something like that, and I said fine, because he is our only witness today and I think he needs some extra time to basically develop his testimony. So with that, we welcome you and thank you.

STATEMENT OF FRANCIS S. COLLINS, M.D., PH.D., DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Dr. COLLINS. Thank you, Mr. Chairman, and thank all of you for those wonderful opening statements. It is clear I am speaking to a very well-informed group of members. I have been looking forward this chance for a conversation for some time and will very much enjoy the questions, and hopefully some answers that occur after a little bit.

But I did want a chance to say something in the way of a introductory set of remarks about NIH. It is a great honor to have a chance to share my vision for the future of biomedical research as we move into the second decade of the 21st century. I have submitted my full written testimony for the record, and I am not going to read from that. I would like to share with you some major themes that were in that statement, and I have a few visuals that will appear up there on the screen.

So I would like to thank this committee for your steadfast support of NIH's mission, which you see here on the slide is twofold: to discover fundamental knowledge about the nature and behavior of living systems, yes, but also to apply that in extension of healthy life and the reduction of the burdens of disability and illness, and has as already been pointed out by a couple of you in your opening statements, we are making real progress there. As you can see, U.S. life expectancy has been climbing over the course of the past few decades, and if you look at disabilities, those also have improved substantially in the course of just the last few years. You can see here the incidence of disability in the elderly has dropped from more than 25 percent back in 1982 to now less than 20 percent. But let me emphasize that human biology is not an end to itself. We wake up every day trying to think about how to further improve those outcomes.

Right now, of course, one of the most urgent goals that everyone is concerned about relates to the BP Deepwater Horizon oil spill. This is an environmental tragedy of unprecedented proportions. For the past several weeks, NIH has been partnering with our sister agencies in the Department of Health and Human Services to protect the health and meet the medical needs of Gulf residents and cleanup workers. For example, the National Institute of Environmental Health Sciences has provided training and safety information to protect the health of responders. Its educational course on hazard awareness and safety is now required for all oil spill workers hired by BP. More than 30,000 to date have been trained by NIEHS including the distribution of a safety handbook. I have a copy here that has been distributed to first-line responders and beach workers.

But we have to do more here, and so today I am announcing that NIH will devote another $10 million in existing funds to support research on the potential human health effects of the oil spill. NIH through NIEHS will recruit a cohort of 15,000 to 20,000 exposed cleanup workers and Gulf residents. We will collect their health histories and tissue samples as well as information about cleanup work they performed and the nature of their exposures. In the near term, NIH will establish a baseline of such information and then we will monitor cohort member for respiratory, immunological and neurobehavioral effects. So that is an example of some urgent responses, and we do feel that is part of our job, to respond to those as they arise.

But we also have to look ahead to tackle our Nation's many ongoing health problems: obesity, cancer, heart disease, diabetes, autism, to name just a few, and you all in opening statements have mentioned quite a number of these. One of my first actions upon being named NIH director was to scan this landscape of biomedical research opportunity to try to identify areas that are really ripe for major advances that could yield substantial benefits in the coming years, and while that list of specific projects could go on forever, I have identified five areas with exceptional opportunity. At your place, there is a reprint of an article in Science magazine and I would like to very briefly tell you what these five themes are that seem particularly ripe now for investments by NIH researchers, and I will go through them one at a time.

First of all, we have seen invented in just the last 4 or 5 years a number of dramatically powerful high-throughput technologies that give us the chance to ask comprehensive questions about how life works, what are all the proteins in the cell, what are all the components of the immune system, what are all the steps in development. We couldn't really ask those questions before and now with technologies like genomics and imaging, computational biology, nanotechnology, we can do those things, and the chance to apply them is really unprecedented in its scope.

A second area that I think is a natural partner to this is to take all those basic science discoveries that are beginning to pour out of our laboratories and accelerate the pace by which those are brought into clinical benefits. NIH traditionally has partnered with the private sector in doing this, and we intend to continue that, but we have the chance now to play an ever-larger role in the front end of drug development pipelines that previously academic investigators didn't get involved in, and we aim to try to push that agenda as quickly as we can in order to take basic science discoveries to the bedside at an unprecedented pace, and by the way, I might say the Common Fund, by the NIH Reauthorization Act, putting it into legislation, is now a major opportunity for me as the NIH director will be investing substantially in both of these areas in the coming years because this is an example of the kind of research that touches on all diseases. It is not limited to any single institute.

A third area is for us to try to provide the kind of evidence that is going to be needed to make wise decisions about health care reform, and that includes things like personalized medicine, pharmacogenomics, comparative effectiveness research. It includes health economics to try to understand how we can better figure out incentives that will both improve outcomes and result in better care.

And at the same time, we also need to think about, and the fourth theme, extending outside of our own boundaries to the rest of the world. We have opportunities in the global arena now to both create and deploy new kinds of diagnostics and therapeutics for AIDS, tuberculosis and malaria and for the neglected tropical diseases that have had relatively little work done upon them but they affect hundreds of millions of people.

And finally, the fifth of the five themes is our own research community, probably our most critical resource. We certainly will depend upon these wonderfully bright minds in order to make these discoveries in the coming years and we need to be sure that we encouraging the best and brightest of the next generation to come and join us, that we are inspiring innovation and not just crank turning, that we are improving the diversity of our workforce, and I might also say that we are encouraging and stimulating and insisting upon the integrity of the process to be at the highest level.

Let me just say a word about that. In the process of overseeing NIH research, one of my priorities to be sure that we are vigilant about managing any potential conflicts of interest or even the appearance of such conflicts. I am determined that NIH should lead in this area, and that is why we are in the midst of proposing a new set of regulations that will require more complete disclosure from NIH-funded investigators about their dealings with industry

in order to maintain the public trust. The need for enhanced trust of financial conflicts of interest has been made particularly salient by the news last week that described a particularly egregious case of failure of an investigator to disclose. In this case the scientist was sanctioned by his university but then went on to move to a new university and thus evaded the sanctions. We are going to fix this problem. The pending notice of proposed rulemaking about conflicts of interest gives us an opportunity to address cases where there are such violations of NIH and university financial disclosure rules. We can clarify our options for enforcement actions against both individuals and institutions. So I am committed to making sure that we earn the public trust and ensure the highest standards of research integrity and transparency.

Now I want to go on to share several exciting examples of how NIH-funded researchers are using some of these revolutionary tools and technologies to expand our understanding of human biology. The more we learn about how the body works, the greater our ability to transform that knowledge into cures and treatments for the many diseases that plague humankind.

Alzheimer's disease has already been mentioned. Currently, more than 5 million Americans suffer from this degenerative brain disorder, and with the aging of the American population, that number could more than double by 2050 and would greatly increase the disease's already steep financial toll. If current trends continue, the annual health care costs associated with Alzheimer's disease would rise from $172 billion to more than $1 trillion over the next 40 years.

Now, because Alzheimer's disease has proved to be such a tough opponent, researchers are now attempting to fight it on many fronts, and the first prong of attack is an interesting one that might not have seemed obvious a couple of years ago, and that is immunotherapy. This involves enlisting the body's own immune system to prevent the accumulation of beta amyloid, which is the protein thought to be a major culprit in Alzheimer's disease. About a decade ago, there was much excitement about a clinical trial of the vaccine but enthusiasm flagged when some participants developed brain inflammation, obviously a serious side effect. Since then, much work has been devoted to figuring out ways to improve the safety profile of such vaccines. One new approach which combines immunotherapy with anti-inflammatory agents has produced encouraging results so far in animal tests. Other recent work by NIH-funded researchers has uncovered a possible new drug target for Alzheimer's disease and one which interestingly brings this disease into closer molecular harmony with Parkinson's disease and with Huntington's disease and a few others. In a study just published last week, researchers describe how a particular gene that is associated with Alzheimer's, presenilin 1, acts to cause this disorder, and interestingly, what they learned was that this protein normally helps clear debris from the brain but mutations block the normal plan for the trash pickup system in the brain, leading to a potentially toxic accumulation of discarded proteins. We already know of a few drugs that would stimulate the trash pickup, and this is raising new ideas about an approach to Alzheimer's that people have not thought about before.

A third effort, and this is a public-private partnership, is the Alzheimer's Disease Neuroimaging Initiative, which is combining various clinical neuroimaging, genetic and spinal fluid measures to understand the events that lead from normal cognition to Alzheimer's disease to finding biomarkers. Such data have been rapidly made available to the worldwide research community and now thanks in this case to an infusion of Recovery Act dollars from NIH, this initiative, ADNI is stepping up its efforts even further.

I also want to talk about cancer. Several of you have mentioned it already. A major project that has been accelerated by Recovery Act funds is this cancer genome atlas, or TCGA. Already, TCGA has produced comprehensive molecular classification systems for ovarian cancer and for glioblastoma, which is the most common form of brain cancer and a very serious one. The team survey of glioblastoma recently revealed five new molecular subtypes of the disease that we didn't know existed before. In addition, researchers found that responses to therapy for glioblastoma vary by subtype and that may help doctors do a better job of matching individual patients with the therapies are most likely to work for them. What is more, the findings may lead to new therapies directed at the molecular changes underlying each type of glioblastoma, providing targets that we very much need to have in order to develop the next generation of therapy.

So now in the next phase of the project, again encouraged by the Recovery Act, TCGA will build comprehensive catalogs of the key genomic changes in 20 major types and subtypes of cancer including gastric cancer. These data are being shared rapidly with the worldwide scientific community and will provide powerful new clues for all who strive to develop better ways to diagnose, treat and prevent cancer.

Those are general stories, but to give you a real-life example, I would like to share the story of Beverly Sotier. When she was diagnosed with stage IV non-small-cell lung cancer several years ago, this nonsmoker was told she probably had 6 months to live. Beverly received standard chemotherapy but her tumors kept growing. Devastating news for her and her children and grandchildren. But then last July based on a genetic analysis of her tumor at the Dana Farber Cancer Institute in Boston, she signed up for a clinical trial of a new genome-based drug called crizotinib. Now, look at the scans. It may be a little hard to see where you are but maybe the red circles will help you, but if you look on the left in both of those images, her lungs, the black areas, have big white spots in them. Those are large tumors growing in her lungs. On the right is after treatment some 5 months later, and those tumors are essentially gone. So she has had a dramatic result, and in the first 6 months of treatment most of her tumors have disappeared.

But this doesn't work for everyone. This particular drug actually seems only to be successful for about 5 percent of people with lung cancer, but we know now which 5 percent because, you see, this drug works on specific genomic changes called a fusion of a gene called ALK with another gene. If your lung cancer has that fusion, this is the drug for you because most of those patients, about three-quarters of them, respond dramatically to this new therapy. This was just announced a few days ago at the American Society for

Clinical Oncology. People in the room were blown away by this kind of response and by the ability to make such a precise prediction about who was going to respond. So this demonstrates the potential of personalized medicine, of the value of matching the right treatment with the right patient at the right time.

Interestingly, Beverly's story also points out rapidly this can happen. When she was first diagnosed, nobody knew about this genomic change in lung cancer. That was discovered just 3 years ago and now here she is showing this dramatic response to a new drug. So it need not be the case that the new therapeutics take many, many years. Clearly, we need a lot more stories like Beverly's, not only for cancer but for asthma, diabetes, depression, heart disease and many other conditions. The brochure you have at your place outlines some of those exciting advances.

So it is my hope and my expectation, Mr. Chairman, that NIH-funded research will bring us much closer to turning discovery into health for all Americans and to do so quickly. If our Nation is bold enough to act today upon the many research opportunities that lie before us, I believe we will all be amazed at what tomorrow brings.

Thank you very much, and I would be glad to answer your questions.

[The prepared statement of Dr. Collins follows:]

Testimony
before the
Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives

Statement for hearing entitled, "NIH in the 21st Century: The Director's Perspective"

Statement of
Francis S. Collins, M.D., Ph.D.
Director
National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 1:00 p.m.
June 15, 2010

Good morning, Mr. Chairman and distinguished Members of the Subcommittee:

It is an honor to appear before you today to discuss the state of the National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services (HHS), and my vision for the future of biomedical research.

First, I'd like to thank this Subcommittee for its steadfast support of NIH's mission: discovering fundamental knowledge about living systems and then applying that knowledge to fight illness, reduce disability, and extend healthy life. NIH is grateful for the confidence that Congress has in our ability to advance this mission. I had the privilege to appear before this Committee in the past as Director of the National Human Genome Research Institute, and I appreciated the opportunity to contribute to your pivotal work on the landmark Genetic Information Nondiscrimination Act. Now, as steward of NIH's entire research portfolio, I look forward to working together with you to explore the frontiers of biomedical research to improve America's health.

I returned to NIH as Director in August of last year, and am extremely proud to stand at the helm of the most significant institution supporting biomedical research in the world. Begun as a one-room Laboratory of Hygiene in 1887, the National Institutes of Health (NIH) today has grown into a complex and multidisciplinary engine for discovery and innovation, comprised of 27 different Institutes and Centers. More than four-fifths of the NIH budget is devoted to funding competitive grants that support more than 325,000 research personnel at more than 3,000 institutions, which are located in all 50 states, the territories, and more than 90 countries around the world. More than 130 researchers funded by NIH have gone on to win Nobel Prizes.

NIH funds research only after the completion of a two-tiered review process, which is considered the "gold standard" of scientific review. Peer review panels comprising external experts evaluate the scientific merit of grant applications and then

Institute advisory councils consider how well the applications address the Institute's mission and programmatic priorities. The process is highly rigorous and competitive; currently, about one application in five is funded.

One of my first actions upon being named NIH Director was to scan this vast landscape of biomedical research for areas ripe for major advances that could yield substantial benefits in coming years. I found many of the most exciting opportunities could be grouped under five main themes: taking greater advantage of high-throughput technologies; accelerating translational science, that is, turning discovery into health; helping to reinvent health care; focusing more on global health; and reinvigorating the biomedical research community. With Congress' support, we are poised to take greater advantage of these unprecedented opportunities, all with the aim of helping people live longer, healthier, and more rewarding lives.

THE RESEARCH MARATHON: HOW FAR WE'VE COME

Our nation's biomedical research effort is in a race that we cannot afford to lose. Science is not a 100-yard dash. It is a marathon – a marathon run by a relay team that includes researchers, patients, industry experts, lawmakers, and the public. Thanks to discoveries funded through NIH appropriations, we have covered a lot of distance in this marathon. Let us take a moment to look back at a few of the advances made possible by NIH-supported research, and then look ahead to some of our nation's biggest health challenges and how NIH intends to meet them.

U.S. life expectancy has increased dramatically over the past century and still continues to improve, gaining about one year of longevity every six years since 1990. A

baby born today can look forward to an average life span of nearly 78 years, almost three decades longer than a baby born in 1900.[1,2]

Not only are people living longer, they are staying active longer. From 1982 through 2005, the proportion of older people with chronic disabilities dropped by almost a third, from 27% to 19%.[3]

We have made some of the most impressive gains against cardiovascular disease. In the mid-20th century, cardiovascular disease caused half of U.S. deaths, claiming the lives of many people still in their 50s or 60s.[4] Today, the death rate for coronary heart disease is more than 60% lower -- and the death rate for stroke, 70% lower – than in the World War II era.[5,6]

What prompted these improvements? One major contributor has been the insights from the NIH-funded Framingham Heart Study, which began in the late 1940s and is still going strong. This population-based study, which changed the course of public health by identifying key risk factors for heart disease, will break new ground with the recent addition of detailed genetic analyses to the research project.

---

[1] National Vital Statistics Reports, Volume 57, Number 14 April 17, 2009. Deaths: Final Data for 2006. Available at: http://www.cdc.gov/nchs/fastats/lifexpec.htm.

[2] "Life Expectancy at All Time High; Death Rates Reach New Low, New Report Shows," CDC Online Newsroom, Press Release. Available at: http://www.cdc.gov/media/pressrel/2009/r090819.htm.

[3] Manton KG, Gu X, Lamb VL. Change in chronic disability from 1982 to 2004/2005 as measured by long-term changes in function and health in the U.S. elderly population. *Proc Natl Acad Sci U S A.* 2006;103:18374-9. Epub 2006 Nov 13.

[4] Fox, CS, et al. Temporal trends in coronary heart disease mortality and sudden cardiac death from 1950 to 1999: the Framingham Heart Study. *Circulation* 2004;110:522-527.

[5] Decline in Deaths from Heart Disease and Stroke—United States, 1900–1999. *MMWR.* 1999;48(30):649-656.

[6] NHLBI Morbidity and Mortality: 2009 Chart Book on Cardiovascular, Lung, and Blood Diseases, page 23.

NIH-supported research also led to minimally invasive techniques to prevent heart attacks and to highly effective drugs to lower cholesterol, control high blood pressure, and break up artery-clogging blood clots. NIH-funded science has also helped people make lifestyle changes that promote health, such as eating less fat, exercising more, and quitting smoking.

Many chronic conditions begin as part of the aging process. One such disease, osteoporosis, can result in life-threatening bone fractures among older people. NIH-funded research has led to new medications and management strategies for osteoporosis that have reduced the hospitalization rate for hip fractures by 16% since 1993.[7] Science has also transformed the outlook for people with age-related macular degeneration, a major cause of vision loss among the elderly. Twenty years ago, we could do little to prevent or treat this disorder. Today, because of new treatments and procedures based in part on NIH research, 1.3 million Americans at risk for severe vision loss over the next five years now can receive potentially sight-saving therapies.[8]

Biomedical research also has benefitted those at the beginning of life. NIH-funded research has given hearing to thousands of children who were born profoundly deaf. Their hearing is made possible with a cochlear implant, an electronic device that mimics the function of cells in the inner ear. Since HHS's Food and Drug Administration (FDA) approved cochlear implants for pediatric use in 2000, more than 25,000 children have received the devices, enabling many to develop normal language skills and succeed in mainstream classrooms.[9]

---

[7] Fatalities and Injuries from Falls Among Older Adults --- United States, 1993--2003 and 2001--2005. *MMWR*. 2006;55(45);1221-1224.

[8] Bressler, NM, et al. Potential public health impact of age-related eye disease study results: AREDS report no. 11. Arch Ophthalmol. 2003 Nov; 121(11):1621-4.

[9] Francis HW, Koch ME, Wyatt JR, Niparko JK. Trends in educational placement and cost-benefit considerations in children with cochlear implants. *Arch Otolaryngol Head Neck Surg*. 1999;125:499-505.

Then, there are the infectious diseases – diseases that respect no boundaries in today's globalized economy or when it comes to age, sex, or physical fitness. One of NIH's greatest achievements over the past 30 years has been to lead the global research effort against the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) pandemic. Building discovery upon discovery, researchers first achieved fundamental insights about how HIV works, and then went on to develop rapid HIV tests, identify a new class of HIV-fighting drugs, and, ultimately, figure out how to combine those drugs in life-saving ways. While the battle against HIV/AIDS continues, today, HIV-infected people in their 20s who receive combination therapy may expect to live to age 70 or beyond.[10]

CONTINUING THE RACE: HOW FAR WE HAVE TO GO

Although we have accomplished much, the opportunities for advancing human health that we see in front of us have never been greater.

Consider the challenges posed by cancer. This disease still claims the lives of more than 500,000 Americans annually – about one every minute.[11] But in 2007, for the first time in our nation's history, the absolute number of cancer deaths in the U.S. went down.[12] And, over the past 15 years, cancer death rates have dropped 11.4% among women and 19.2% among men, which translates into some 650,000 lives saved – more than the population of Washington, D.C.[13] Such progress is even more striking when one considers that many cancers are strongly associated with aging, and that the U.S. population is growing increasingly older. These are encouraging milestones, but they are not nearly enough.

---

[10] Cooper DA.Life and death in the cART era. *Lancet*. 2008;372:266-7.

[11] American Cancer Society. Cancer Facts and Figures 2006. Available at: http://www.cancer.org/downloads/STT/CAFF2006PWSecured.pdf.

[12] McCarthy, M. Number of Cancer Deaths Continue to Fall in the United States. *Lancet* 2007;369: 263.

[13] American Cancer Society. Cancer Death Rates Steadily Declining.. Available at: http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Cancer_Death_Rate_Steadily_Declining.asp.

NIH-funded research has revolutionized how we think about cancer. A decade or two ago, cancer treatment was mostly reactive; diagnosis was based on the organ involved and treatment depended on brute force therapies that were highly toxic and often greatly diminished the patient's quality of life. Today, basic research in cancer biology is moving treatment toward more effective, targeted, and less toxic therapies tailored to the genetic profile of each patient – and each patient's cancer.

Among the early success stories in this area is the drug trastuzumab (Herceptin) for breast cancer. An NIH-sponsored clinical trial studied the effectiveness of trastuzumab combined with standard chemotherapy in reducing recurrence of the disease. The trial found that breast cancer patients whose tumors have certain genetic markers indicating a responsiveness to trastuzumab reduced their risk of cancer recurrence by 52%.[14] That improvement is the best ever reported in post-surgical treatment of breast cancer. Studies also have found that the chemotherapy drugs gefitinib (Iressa) and erlotinib (Tarceva) work much better in the subset of lung cancer patients whose tumors have a certain genetic signature.[15,16]

To accelerate the development of more individualized strategies for more types of cancer, NIH has tapped into the promise of high-throughput technologies and launched The Cancer Genome Atlas (TCGA). Over the next few years, TCGA's research team will build comprehensive catalogs of the key genomic changes in 20 major types and subtypes of cancer. These data are being shared rapidly with the worldwide scientific community, and will provide powerful new guides for all those striving to develop better ways to diagnose, treat, and prevent cancer.

---

[14] Romond EH, Perez EA, Bryant J. et al. Trastuzumab plus adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med*, 2005;353:1659-1672.

[15] Feld R, Sridhar SS, Shepard FA et al. Use of the epidermal growth factor receptor inhibitors gefitinib and erlotinib in the treatment of non-small cell lung cancer: a systematic review. *J Thorac Oncol*. 2006;1: 367-76.

[16] Gazdar AF. Epidermal growth factor receptor inhibition in lung cancer: the evolving role of individualized therapy. *Cancer Metastasis Rev*. 2010;29: 37-48.

Already, TCGA has produced a comprehensive molecular classification system for ovarian cancer and glioblastoma, which is the most common form of brain cancer. Our survey of glioblastoma recently revealed five new molecular subtypes of the disease. In addition, researchers found that responses to aggressive therapies for glioblastoma varied by subtype. These findings hold the promise that we can match the most appropriate therapies to individual brain cancer patients and may also lead to therapies directed at the molecular changes underlying each subtype, as we are already able to do for some types of breast cancer.

Diabetes is another disease that is devastating our nation's health. More than 23 million Americans currently have diabetes – nearly 8% of the population.[17,18,19,20] Another 57 million adults have blood sugar levels that indicate they are at serious risk of developing the disease, which is a major cause of kidney failure, stroke, heart disease, lower-limb amputations, and blindness.[21,22,23]

For type 2 diabetes, prevention appears to be the name of the game. This form of the disease, which accounts for more than 90% of cases, often can be averted or delayed

---

[17] Cowie CC, Rust KF, Byrd-Holt DD, Eberhardt MS, Flegal et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health And Nutrition Examination Survey 1999-2002. *Diabetes Care.* 2006;29:1263-8.

[18] NHANES 2003–2006, National Center for Health Statistics, Centers for Disease Control and Prevention. Available at: http://www.cdc.gov/nchs/nhanes.htm

[19] 2004–2006 NHIS, National Center for Health Statistics, Centers for Disease Control and Prevention. Available at: http://www.cdc.gov/nchs/nhis.htm

[20] U.S. Census Bureau, resident population estimates for 11/1/2007. Available at: http://www.census.gov/popest/national/asrh/2006_nat_res.html.

[21] Cowie, 1264-1265.

[22] NHANES 2003–2006.

[23] U.S. Census Bureau, resident population estimates for 11/1/2007.

by lifestyle changes.[24] The NIH-funded Diabetes Prevention Program (DPP) trial showed that one the most effective ways to lower the risk of type 2 diabetes is through regular exercise and modest weight loss.[25] There is good reason to believe that such efforts may lead to a lifetime of additional health benefits. A recent follow-up study of DPP participants found the protective effects of weight loss and exercise persist for at least a decade.[26] NIH also led research efforts to explore ways to implement DPP findings in real-world settings at lower cost, such as in YMCAs. The United Health Group has recently announced a partnership with YMCAs and Walgreen's pharmacies to implement on a national scale what we have learned from this groundbreaking NIH-funded research.

More than one-third of adults in the U.S. are obese, according to the latest data from the National Health and Nutrition Examination Survey, which is conducted by the Centers for Disease Control and Prevention (CDC).[27] And there are troubling signs that the next generation may face an even greater struggle. Over the past 30 years, obesity has more than doubled among U.S. children aged 2 through 5 and nearly tripled among young people over the age of 6.[28,29] These statistics mean that tens of millions of Americans face an increased risk of type 2 diabetes, as well as cardiovascular disease, high blood pressure, certain cancers, osteoarthritis, and other serious health problems associated with excess body fat.

---

[24] National Diabetes Fact Sheet, 2007. Available at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf

[25] Diabetes Prevention Program Research Group. Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin. *N Engl J Med.* 2002;346:393-403.

[26] Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, Hamman RF, Christophi CA, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet.* 2009;374:1677-86. Epub 2009 Oct 29. Erratum in: *Lancet.* 2009;19;374:2054.

[27] Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. *JAMA.* 2010;303:235-41. Epub 2010 Jan 13.

[28] Ogden CL, Carroll MD, Curtin LR, Lamb MM, et al. Prevalence of high body mass index in US children and adolescents, 2007-2008. *JAMA.* 2010;303:242-9. Epub 2010 Jan 13.

[29] Health E-Stat, June 2010. Available at: http://www.cdc.gov/nchs/data/hestat/obesity_child_07_08/obesity_child_07_08.htm,

To fight America's obesity epidemic, NIH has launched a variety of initiatives aimed at developing innovative approaches for weight control. One such effort, called the National Collaborative on Childhood Obesity Research, has pulled together experts from four NIH Institutes, the CDC, and the Robert Wood Johnson Foundation. An example of their work is the Trial of Activity for Adolescent Girls, a national study to develop and test school- and community-based interventions to get girls more involved in gym class, organized sports, or recreational activities. Another NIH program, called *We Can!*, provides families with practical tools for weight control at more than 1,000 community sites nationwide.

Meanwhile, other NIH-funded researchers are busy uncovering information about genes and environment that might point the way toward more personalized, targeted strategies for controlling weight and preventing diabetes. For example, in just the past few years, we have identified more than 30 genetic risk factors for type 2 diabetes.

Uncovering possible genetic factors may also help address the urgent demographic reality of Alzheimer's disease (AD). In the United States, it is estimated that as many as 5.1 million people may have Alzheimer's, and by 2050, with the aging of the baby boomers, that number could double.[30] In a relentless search to find ways to slow down or prevent AD, the NIH is employing a variety of new technologies and approaches to identify genes that may play a role in risk of late-onset Alzheimer's. Through various clinical, neuroimaging, genetic, and fluid biomarker measures to assess the sequence of events in the brain which leads from normal cognition to AD, a public-private partnership called the AD Neuroimaging Initiative is showing some success in finding methods for early diagnosis and assessing whether drugs and other interventions can prevent or delay the onset of AD. Since 2006, NIH has funded close to 60 AD translational research projects that support early drug discovery and preclinical drug development for AD and age-related cognitive decline.

---

[30] Hebert LE, Scherr PA, Bienias JL et al. Alzheimer disease in the U.S. population: prevalence estimates using the 2000 census. Arch Neurol 60: 1119-1122, 2003.

A better understanding of genetic and environmental factors may help solve a frustrating medical puzzle: the causes of autism. Children with autism spectrum disorders experience a range of problems with language and social interactions, sometimes accompanied by repetitive behaviors or narrow, obsessive interests. Recent studies funded by NIH have associated autism risk with several genes involved in the formation and maintenance of brain cells, but much more work is needed to follow these clues.

Now and in coming years, NIH will support comprehensive and innovative approaches to piece together the complex factors that contribute to autism spectrum disorders. One ambitious effort will involve sequencing the complete genomes of 300 people with autism and their parents. Other researchers will examine mothers' exposures during pregnancy to identify possible environmental factors. NIH hopes to use these insights to develop new molecular and behavioral therapies for such disorders, as well as identify possible strategies for prevention.

Another brain disorder, depression, presents a different set of challenges. Although researchers have made significant progress in understanding the biology of depression, improving treatment, and lessening the social stigma associated with mental illnesses, suicide is the fourth leading cause of death among young people between the ages of 15 and 24.[31] Untreated depression can also reduce productivity, cause family stresses, and increase the risk for serious health problems, such as substance abuse and heart disease.

How can medical research reduce depression's tragic toll? One way is to recognize that this is a brain disease, and to seek out its molecular underpinnings. Researchers today are using functional magnetic resonance imaging and other innovative technologies to see how the brains of people with depression differ from those without the disorder. Another critical need is optimizing therapy. Finding the

[31] http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58-14.pdf

right antidepressant drug for any particular patient currently is a lengthy, trial-and-error process that can take weeks or months before symptoms are relieved. NIH supports laboratory research aimed at developing quicker-acting antidepressants, as well as genetic studies that will help to match individuals with the drugs most likely to work for them.

In 2009, 160 U.S. active-duty soldiers committed suicide – the highest level since the Army began keeping records three decades ago.[32] To address and prevent these tragedies, NIH and the U.S. Army recently partnered to launch the largest study ever of suicide and mental health among military personnel. The Army Study to Assess Risk and Resilience in Service Members (Army STARRS) will identify risk factors that may enable us to develop more effective approaches to suicide prevention.

TRANSFORMING DISCOVERY INTO HEALTH

Whatever the disease, be it depression, diabetes, or something much rarer, NIH's emphasis today and beyond will be on translating basic discoveries into new diagnostic and treatment advances in the clinic.

Of course, that kind of translation must be built upon a vigorous foundation of basic science research supported by NIH – or else there will be nothing to translate. A few decades ago, when researchers began studying a rare hereditary disorder that resulted in very high cholesterol levels, some might have argued that this basic investigation of lipid metabolism was rather obscure and irrelevant to the medical care of most of the population. But out of that research came the understanding of how cholesterol is synthesized in the liver, and a direct consequence was the development of a class of drugs, known as statins, which has saved countless lives from heart disease.

[32] http://www,defense.gov/releases/release.aspx?releaseID=13525

Today, there are unprecedented discoveries coming from basic research that have been made possible by the emergence of fields such as genomics, and technological advances such as high throughput technologies. These opportunities will ultimately lead to breakthroughs in our understanding of the causes of many diseases and to new targets and pathways for potential treatments. What makes these opportunities so extraordinary is that they enable us to take a much more comprehensive approach to human biology. Now, we can focus on *all* of the genes, proteins, and pathways in a molecular and cellular network, enabling a thorough elucidation and understanding of their roles in multiple disease processes.

For many disorders, these new insights into molecular mechanisms represent new opportunities for NIH to shorten and straighten the pathway from discovery to health. This expectation is grounded in several recent developments: the dramatic acceleration of our basic understanding of hundreds of diseases; the establishment of NIH-supported centers that enable academic researchers to use such understanding to screen thousands of chemicals for potential drug candidates; and the emergence of public-private partnerships to aid the movement of drug candidates identified by academic researchers into the commercial development pipeline.

Let me give you one exciting example of how NIH will implement this strategy: the Therapeutics for Rare and Neglected Diseases (TRND) program. This effort will bridge the wide gap in time and resources that often exists between basic research discoveries and the human testing of new drugs.

A rare disease is one that affects fewer than 200,000 Americans. However, if all 6,800 rare diseases are considered together, they afflict more than 25 million Americans. Private companies seldom pursue new therapies for these types of diseases because of the high cost of research and low likelihood of recovering their investments. Effective drugs exist for only about 200, or less than 3%, of these rare diseases. But not all neglected diseases are rare. Some of these diseases affect hundreds of millions of people who live in low income countries, but, because of lack of economic incentives,

there is a dire shortage of effective, affordable treatments for these major global causes of death and disability.

Working in an open environment in which all of the world's top experts on a disease can be involved, TRND will enable certain promising compounds to be taken through the preclinical development phase – a time-consuming, high-risk phase often referred to as "the valley of death" by pharmaceutical firms focused on the bottom line. Besides speeding development of drugs for rare and neglected diseases, TRND will serve as a model for therapeutic development for common diseases, many of which are being resolved into smaller, molecularly distinct subtypes.

NIH is taking other steps to re-engineer the pipeline that connects all of the points between the identification of a potential therapeutic target by a basic researcher and FDA approval of a therapeutic for clinical use. Among our new tools is the NIH Clinical and Translational Sciences Award program, which currently funds 46 centers in 26 states, and will add more this year. This national network is pulling together interdisciplinary clinical research teams to work in unprecedented ways to develop and deliver tangible health benefits. Another powerful resource for translation is the nation's largest research hospital, the Mark O. Hatfield Clinical Research Center, located on the NIH campus in Bethesda, MD. Just as they blazed a trail for safe and effective human gene therapy, NIH clinical researchers may be well positioned to discover other pioneering approaches to human therapeutics, such as those using human embryonic stem cells or induced pluripotent stem cells derived from skin cells.

To make the most of these new opportunities, the NIH and FDA recently forged a landmark partnership with the formation of a Joint Leadership Council. Members of this Leadership Council will work together to ensure that regulatory considerations form an integral component of biomedical research planning, and that the latest science is integrated into the regulatory review process. Such collaboration will advance the development of products to treat, diagnose and prevent disease, as well as enhance the safety, quality, and efficiency of clinical research and medical product approval.

NIH REFORM ACT

The NIH Reform Act of 2006, which was conceptualized, crafted, and codified through the efforts of this Subcommittee during the 109th Congress, provided NIH with two key tools for optimizing the use of scientific and funding resources. We have fully implemented this landmark legislation, and I would like to provide you with an update on two of these key features: The Common Fund and the Scientific Management Review Board.

The Common Fund fosters collaboration and interdisciplinary research, allowing NIH to bring the best minds together to solve the most complex problems and stimulate innovation. For example, The Common Fund's Molecular Libraries program gives academic researchers access to large-scale screening capacity similar to that found at publicly funded, mid-sized pharmaceutical companies, empowering them to move their research beyond basic discoveries into the early components of the drug development pipeline. More than 100 promising new compounds have already been identified through this program.

Another large-scale effort funded through the Common Fund, the Human Microbiome Project, several weeks ago published its analysis of the genomes of 178 types of microbes that live in or on the human body.[33] The researchers discovered novel genes in these microbes, adding a new level of understanding to what we know about these microorganisms and how they contribute to human health and disease.

By authorizing the NIH Common Fund, this Subcommittee underscored NIH's need for flexibility to plan and adjust research priorities based on public health needs and scientific opportunities. The Subcommittee also recognized that some of the most promising new approaches to biomedical research have potential applications to multiple diseases and organ systems, and, therefore, can be difficult to fund through the usual priority-setting processes of the 27 Institutes and Centers. The Common Fund has

[33] *Science* 21 May 2010 Vol. 328. no.5981, pp. 994-999

provided an exciting and powerful new source of "venture capital" for such crosscutting and innovative initiatives.

The NIH Reform Act also created a key advisory committee, the Scientific Management Review Board (SMRB), through which outside experts provide advice to the NIH Director on the organizational structure of NIH, with a specific focus on whether modifications to the structure are needed to optimize the management of scientific funds and resources. The SMRB is currently addressing organizational questions related to the management of research on substance use, abuse, and addiction and carrying out a comprehensive review of the role and structure of the NIH intramural program, including the Clinical Center. The Board has also developed a framework for considering organizational change, which will be used to guide its work.

BIOMEDICAL RESEARCH PROPELS U.S. ECONOMY

Investing in NIH not only improves America's health and strengthens our nation's biomedical research potential, it propels the U.S. economy. Consider the following statistics:

- A report issued by Families USA estimated that in 2007, every $1 in NIH funding resulted in an additional $2.11 in economic output in the U.S.[34]
- In FY 2007, a typical NIH grant supported the salaries of about 7 primarily high-tech jobs in full or in part.[35] The 351,000 jobs resulting from NIH awards paid an average annual wage of more than $52,000 per annum and account for more than $18 billion in wages for FY 2007.[36]

---

[34] FamiliesUSA (2008). In Your Own Backyard: How NIH Funding Helps Your State's Economy. Washington, DC. Available at: http://www.familiesusa.org/issues/global-health/publications/in-your-own-backyard.html.

[35] McGarvey, W. E., P. Morris, et al. (2008). How Many Scientists Do the NIH Support? Improving Estimates of the Workforce. Available at: http://report.nih.gov/FileLink.aspx?rid=530.

[36] FamiliesUSA (2008). In Your Own Backyard.

- Long term, NIH funded R&D sparks U.S. economic innovation in the high-technology and high value-added pharmaceutical and biotechnology industries. For example, between 1982 and 2006, one-third of all drugs and nearly 60 percent of promising new molecular entities approved by the FDA cited either an NIH-funded publication or an NIH patent.[37]
- One study estimated that taking into account the multiplier effect of jobs created in other sectors by NIH-supported research, biopharmaceuticals supported total employment of 3.2 million jobs in 2006, including 686,442 direct jobs and significant source of employment in the U.S. economy.[38]
- NIH-funded research has contributed to overall gains in average U.S. life expectancy from 1970 to 2000 that were worth an estimated $95 trillion.[39]

IMAGINE THE FUTURE

If our nation is bold enough to exploit today's unprecedented opportunities in biomedical research, we will be amazed at what tomorrow brings.

In the world I envision just a few decades from now, the one-size-fits-all approach to medicine will be a thing of the past, and we will use genetic information and environmental exposure data to personalize health care strategies. Doctors will use a patient's genetic profile – not just weight or age – to determine the best drug and the optimal dose. Even prevention strategies, such as exercise or diet, will be tailored to each person's unique genetic makeup and environmental circumstances.

---

[37] Lichtenberg, F. R. and B. Sampat (2008). The Contribution of NIH-supported research to pharmaceutical-embodied technological progress. NIH Office of Science Policy Analysis.

[38] Lawton R. Burns, PhD."The Biopharmaceutical Sector's Impact on the U.S. economy: Analysis at the Nationa, State, and Local Levels, " Archstone Consulting. March, 2009 http://www.archstoneconsulting.com/biopharmapdf/report.pdf

[39] Murphy, K. M. and R. H. Topel The value of health and longevity. *Journal of Political Economy*. 2006; 114: 871-904.

We will use stem cells to repair spinal cord injuries, bioengineered tissues to replace worn-out joints, genetic information to tailor therapies with individualized prescriptions, and nanotechnology to deliver these prescriptions with exquisite precision. We will be able to address in unprecedented ways maladies such as diabetes, cancer, and cardiovascular disease, which have affected friends or family of all of us in some way. Contemplate these possibilities:

- An artificial pancreas – perhaps an implantable device – will automatically sense a person's blood sugar and adjust insulin dosage precisely, and stem cell research may lead to the ability to replace altogether failing insulin-producing cells.
- Oncologists will select cancer drugs based on the precise DNA changes in each person's tumor, targeting cancer cells precisely, with limited toxicity to healthy cells.

- Personal gene chips will predict risk for high blood pressure and heart disease, and doctors will routinely use minimally invasive image-guided procedures to preempt heart disease.

I also dream of a day when, in ways yet to be discovered, we will be able to prevent Alzheimer's, Parkinson's, and other diseases that rob us much too soon of family and friends.

Just imagine what such a future would mean for our nation and all humankind. This is what keeps NIH in the research marathon, and why we ask you to go the distance with us.

Thank you Mr. Chairman. That concludes my formal remarks.

Mr. PALLONE. Thank you, Dr. Collins, and we are going to have members ask questions now. Some have 5 and some have 8 if they didn't do an opening statement, and I will start with myself for 5 minutes.

Dr. Collins, I am just regularly visited as you can imagine by families and advocates with very compelling stories about diseases they have grappled with, and of course the message almost always is, please increase NIH research for, you know, the particular disease and particularly of course during the appropriations season, and of course, every one of us has had one disease that may have had a profound effect on our lives either personally or our families. The reason I bring that up is because many of us believe that we should allow science and the public health, not politics, obviously, to determine the research priorities of NIH, and I think that generally speaking, that is true, and that has been the case. But to be sure, there are times when the relationship between national spending, science and public policy have to be considered. Some diseases like Alzheimer's, for example, are responsible for a massive strain on our Medicare and Medicaid programs. Other developmental disabilities like autism have a significant effect on our families from a very young age and on our school budgets and social services programs. Obesity, for example, is skyrocketing and has a major economic impact and is responsible for loss of productivity, restricted activity, absenteeism. The point I am trying to make is that it is difficult because many times the effects of some diseases or disorders has a huge impact on the economy and the question of how much we spend and how many dollars are lost, so it is hard to completely take out funding and politics from the scenario. But what I wanted to ask you is, what factors you consider when formulating NIH budget and how can we best work with you to ensure that NIH is maximizing its research dollars. Do you think that, you know, perhaps we are being too—you know, that we are not giving you enough input or perhaps the way we are going about prioritizing things needs to be changed?

Dr. COLLINS. Thank you, Mr. Chairman. This is certainly an issue that at NIH we discuss probably just about daily, are we getting our priorities right. The factors that go into that are numerous and they do change over time. Certainly the burden of a disease has to be a major consideration. I mentioned Alzheimer's in my opening statement particular because of the concern about the burden this disease places on people today and that it may place on people tomorrow, and if we certainly need breakthroughs in a disease, Alzheimer's is near the top of that list. Sorry, I seem to have a disease myself today. I am trying to struggle with the aftermath of some sort of respiratory virus.

So certainly the burden is one factor, but if we only studied common diseases that affect hundreds of millions of people, then what about the rare diseases? If a rare disease strikes your family, it probably doesn't matter to you too much that it is rare. You hope that somebody will be doing something for that. Gastric cancer was mentioned, which is growing in its frequency and we don't know why, but it is still a rare cancer. Should we ignore it and just study the common cancers? That doesn't sound right either.

Then of course, there is the matter of scientific opportunity. In a circumstance where there has been a new realization of opportunity to make a real advance in a disease, even if that is not as common as a different disease, you wouldn't want to pass that up, so that folds in there. Fortunately, peer review, which NIH does probably better than any organization in the world, is one of the ways of trying to make sure we are using our investment wisely, and we do have a two-level peer review system. The first level is to look at scientific excellence of a proposal but the second level looks at program needs, and there again that is an opportunity for our experts to come to our advisory councils from universities and companies all over the country and sometimes the world to give us advice about should you steer your ship a little bit further in this direction or the other.

The other thing I should say is that basic science not attached to any particular disease is also a critical part of our portfolio and needs to be so because that is the foundation upon which we build the future, and if we solely made decisions on the basis of diseases, we might miss out on those important investments. I guess what I am saying is, it is a very complex calculus and it should be, but I do think it is best made by people who have a sense of the entire landscape. I am sympathetic with what must happen to you every day when someone with a very compelling story where more resources clearly would help in terms of the advances that are needed in research is asking for your help because I have those same conversations all the time, and obviously more resources in many instances would help but we have a limited opportunity here in terms of the budget, the resources that the taxpayers are willing to give us. I do think the best plan is for those decisions to be made on the basis of science, and I think at NIH, not just speaking for myself but for those 27 institute and center directors and all the advisors we have with all of their expertise, I think we do a pretty reasonable job.

Mr. PALLONE. Thank you very much.

Mr. Shimkus.

Mr. SHIMKUS. Thank you, Mr. Chairman. First I would like to ask unanimous consent that we can submit this letter into the record. It is a very historic letter because it is a letter signed by Senator Durbin and myself, and you will not see these letters signed on a similar issue. It is on gastric cancer, as was mentioned by Dr. Collins.

Mr. PALLONE. Historic because Dick Durbin signed it? Is that what you mean?

Mr. SHIMKUS. We both signed the same letter. That is why it is historic.

[The information appears at the conclusion of the hearing.]

Mr. PALLONE. Oh, I see. Without objection, so ordered.

Mr. SHIMKUS. Thank you, Mr. Chairman, and welcome.

I want to commend NIH's commitment and emphasis on this translational research and to give basic researchers a tool to covert their discoveries into therapies for patients. This, I believe, is one of the most important parts of the research, that part that makes a difference in patient survival. How do you hope to expand NIH and NCI's work in this area?

Dr. COLLINS. So if the question is about the basic part of cancer research, I think we are at a remarkably exciting time in terms of our understanding of what makes cells grow and what makes them stop growing, and really that is the nature of cancer, is the loss of control that a cell normally has. When you see cells that have lost that control, even in their proper location or worse yet, if they have spread to other parts of the body, that is a malignancy. We have learned a lot in the last 10 or 20 years about the signals that control the on and off switches for cells but we have a lot more to learn there. I am particularly delighted to welcome on July 12th the new director of the National Cancer Institute, Dr. Harold Varmus, who will be coming back to NIH after 10 years after president of the Sloan Kettering Cancer Center in New York and Nobel laureate as he is, and somebody who won his Nobel Prize in this very area, and I think it could hardly be a more exciting time for exploring and finding the additional answers we don't know about yet in terms of the basic understanding of cancer, and that is going to shine a bright light on prevention and treatment strategies.

Mr. SHIMKUS. Great. Thank you. My time is limited. Let me go to—in my opening statement I mentioned in the stimulus bill but also just regular funding the 2-year program versus a 4-year program, and how does that help or how does that hurt, and the real question is, would it have been better in the stimulus bill had we went to longer-term strategies and in the remaining stimulus dollars that haven't been spent would you like the opportunity to be able to shift that to longer-term research programs that you have?

Dr. COLLINS. I appreciate the question. Certainly the availability of support from the Recovery Act was a wonderful opportunity for NIH. We had gone through a 5-year period where the budget had been relatively flat, and that meant inflation had been eroding our buying power to the point where we had lost about 16, 17 percent of our purchasing power, and there was a great pent-up interest and need on the part of the scientific community for new resources to spur innovation. So the availability of those dollars from the Recovery Act resulted in an incredible outpouring of grant applications. One particular kind of application that we designed very quickly and put out there for people to respond to called Challenge Grants. We thought we might get 4,000 or 5,000 applications. We got more than 20,000, and it took quite a lot of work to get the reviews done and decide what we could fund. So clearly there was a need, and I would argue that the dollars that came to NIH from the Recovery Act are extremely well spent. They are going to produce very interesting scientific advances. But you are quite right, that 2 years is a very short cycle time for most scientific projects. I understood, and I think all of us did, why that was the case. We were, after all, and still are in an economic downturn of considerable magnitude, and the point here was not just to do great science but also to encourage job creation and to stimulate the production of goods and services, and I think NIH money has done that really quite remarkably well, 50,000 jobs——

Mr. SHIMKUS. My time is running out, but can you address the remaining stimulus dollars and putting it to longer-term prospects?

Dr. COLLINS. So we have essentially allocated all of our $10 billion. We were given a chance for a few of those dollars to be put into multi-year projects but most of them are in 2-year efforts.

Mr. SHIMKUS. Let me just find an end with this. There is an NIH-funded study called Changing Lanes, Changing Times: The Risks Facing Female Drivers Today. Isn't that better a NHTSA study versus an NIH study? So the question is, what is the process by which you decide to do NIH-funded research that probably should be a NHTSA one versus what you have decided? And it is not an insignificant amount of money. For 2009, it was $7,000 but $260,000 for 2008. So it is a pretty big chunk of change.

Dr. COLLINS. So Mr. Shimkus, I am not familiar with that particular grant. The process we follow——

Mr. SHIMKUS. I think the best way is if you could just come back and give me a response to that later on, I would appreciate it.

Thank you, Madam Chairman.

Ms. DEGETTE [presiding.] Dr. Collins, could you also provide this committee with a copy of the slides that you showed today? Our aging eyes had difficulty seeing over there.

Dr. COLLINS. I would be delighted to, yes.

Ms. DEGETTE. Thank you.

The Chair will recognize Chairman Dingell for 8 minutes.

Mr. DINGELL. Thank you, Madam Chairman. I have a great concern about how NIH addresses its investments in research. We have several considerations that go into this. The first is that some diseases impose an enormous fiscal burden on Medicare, Medicaid and the American people. For example, Alzheimer's costs three times as much to Medicaid as other chronic diseases. In Medicaid, it costs nine times as much. So you have the cost component. Next you have the good scientific approach. In other words, which is best to go into from the scientific standpoint. And then there are some other considerations, one of which is we confront the problem of the deep concerns of people who have this as a part of their experience, the disease. And how do you prioritize stopping of high-cost diseases like Alzheimer's and how do you mix these concerns?

Dr. COLLINS. So Mr. Dingell, I think that has been one of the strongest mandates that I as the NIH director and the other 27 institute and center directors share is the need to look at those priorities and to try to balance those considerations between the burden of the disease, which means how serious is it, how many people does it affect, what is its cost to society, what is its personal cost to the individual and to the family but also factor into that the scientific opportunities which may in some instances be more ripe than in others. As I said earlier, I think that we also have to be sure we are not neglecting those rare diseases which are in many instances opportunities not only to help people who are suffering from a condition that might otherwise be a bit neglected but often shed light on common diseases. We would not, for instance, right now have the statin drugs had not been for the study of a rare disease called familial hypercholesterolemia that Brown and Goldstein, who later won the Nobel for this, figured out this whole pathway that led to the discovery of statins.

Mr. DINGELL. Do things like we have done with regard to viruses and genetic research which enabled you to address the questions

that would lead us, for example, to a cure for polio. But let us come back. How do you prioritize addressing diseases like Alzheimer's and how do you balance this against the scientific opportunities and how at the same time do you deal with the problems of getting the biggest bang for your buck while at the same time doing the best job we can in areas? And to come back to Alzheimer's, what about the situation? How much are we putting into Alzheimer's and how are we evaluating what we are doing there?

Dr. COLLINS. So Alzheimer's disease is particularly an emphasis at the National Institute on Aging but several institutes at NIH invest in Alzheimer's research. In 2009, $534 million of NIH money was put into this, and that includes $77 million from the Recovery Act, and that included a wide range of research investigations from such things as the ability to understand the genetic contributions to Alzheimer's going beyond the well-known APOE e4 to other variants that have now been demonstrated as playing a role to new imaging approaches that allow us to assess whether a treatment is working without having to wait years to see if that is the case, biomarkers of response to therapy to immune therapies which are actually looking quite promising as a way to potentially reduce the formation of these beta amyloid plaques to new ideas that suggest maybe a new drug therapy approach. There are 30 drug trials that are either in place or getting ready to go into action in terms of Alzheimer's approaches. So there is a lot of activity here but I share the sense that this is a time bomb. I mean, it is already upon us but it is going to get worse if we don't come up with better strategies for prevention and treatment in the future.

Mr. DINGELL. Let us talk here about cooperation and collaboration with other agencies, which you just mentioned. FDA plays an integral role in the translating basic discoveries into new diagnostic and treatment advances in the clinic. There has to be both a smooth transition and it has to work between discovery and FDA analysis. The Administration is recognizing this and they are recognizing we can do a better job in biomedical research planning and regulatory review of newly discovered therapies. How do you feel this will provide the needed predictability for industry as they make investment decisions?

Dr. COLLINS. Very important question, Mr. Dingell, and certainly from my perspective, the need for close connections between NIH and FDA has never been greater. Accordingly, Peggy Hamburg, the commissioner of the FDA, and myself have established an NIH/FDA leadership council and we had a public input meeting just 10 days ago to see what issues that council might take on, and we have begun a scientific research effort in regulatory science to try to give the FDA some new tools to be able to do review of new and creative research clinical trials in order to speed up the process of assessing whether truly new approaches are safe and effective. I think it is timely indeed to have those kinds of opportunities brought forward, and I think industry is welcoming the way in which Dr. Hamburg has brought the idea of regulatory science into the present time in order to try to handle some of these more creative approaches to design and testing of new therapy.

Mr. DINGELL. Now, I have a further concern here. We have put some money into health reform research tax credits. The new

health reform law provides tax credits to support biological research and biomedical research for small firms, something which you know rather much about from your time at University of Michigan. How helpful do you think this tax credit is going to be in producing new therapies and in addressing unmet medical needs?

Dr. COLLINS. So this is the program called the Qualifying Therapeutic Development program which is supposed to make it possible for biotechnology companies with less than 250 employees to be able to get a tax credit if they are involved in therapeutic or other clinical advances in medicine. I actually think this could be a very useful program at a time where many of these companies are really starved for capital. With the economy in its downturn, venture capital has been hard to come by and so this is a chance for companies that have projects that have stalled for lack of support to be able to obtain tax credits or grants to get those things going again.

Dr. COLLINS. Doctor, there are two questions I want to get in the record here. Why is it important that this credit be targeted to smaller biotech firms, and second, how will the applications be prioritized amongst diseases and amongst the hopefulness of a particular treatment or a particular firm?

Dr. COLLINS. I think the goal particularly was to try to provide relief for small companies who have been dependent on venture capital that is no longer easy to come by. Hence, the reason for small companies. As far as the prioritizing, NIH has been asked to do the reviews of the applications and we have welcomed the chance to do that. We will prioritize on the basis of the likelihood of success of particular projects and the importance therefore of providing additional financial resources to make that happen.

Mr. DINGELL. Thank you, Doctor. My time is up.

Thank you, Madam Chairman.

Ms. DEGETTE. Mr. Gingrey.

Mr. GINGREY. Madam Chairman, thank you.

Dr. Collins, let me ask you a couple of things. You mention in your testimony the promise that high-throughput technologies—that was one of the bullet points on the slide—high-throughput technologies hold for our understanding of the causes of many diseases and new pathways for potential treatment. Can you explain what high-throughput technologies are and how this technology might benefit our health system?

Dr. COLLINS. Certainly. Thank you for the question. High throughput is essentially referred to new approaches that understanding how life works in a cell, usually a human cell, where you don't just look at one protein at a time or one gene at a time or one metabolite at a time. You are trying to look in a very rapid fashion at a very large amount of data. Genomics is one of those high-throughput technologies where we used to satisfy ourselves with focusing in on a single gene that caused, for instance, sickle cell disease, but now we can sequence the entire genome, all 3 billion letters of the code in the space of about a week. That is high throughput. Now, that is a challenge then to be able not just to generate the data but to make sense of it, so another part of high-throughput technologies is a lot of computational needs so that marriage of biology and computers, which has been coming along

for a while, is now really fully underway and a very productive marriage it is indeed.

Mr. GINGREY. Thank you, Dr. Collins. Let me go back to in a way something that Chairman Emeritus Dingell was talking about in regard to how you make the decision on what to fund, and I think the gentleman from Connecticut and the gentlewoman from Tennessee both mentioned about job creation and that sort of thing. When an application is going through the peer review process, how much weight is given to the number of jobs that the grant will support in contrast to, say, what Chairman Emeritus Dingell was talking about Alzheimer's and the significance of that disease on the cost to our overall health care system? How do you balance that?

Dr. COLLINS. So our primary reason for doing that first level of review is to look at the excellence of the science. We want to be sure we are supporting the very best scientific ideas. The second level of review then really looks at program relevance and balance and may very well take some account then into what kind of project is this and how many people would be supported. But frankly, the difference between the types of grants that we would support in this process in terms of how many jobs they would create is not going to be very huge. Most of this will be defined by the dollars that are being invested in research because in general about 30 to 40 percent of our research dollars are going to support the salaries, the jobs of the individuals doing the work. And so whether we pick this grant or that grant——

Mr. GINGREY. I am sorry. What percentage?

Dr. COLLINS. Thirty to 40 percent, somewhere in that neighborhood of what we are spending in terms of our direct costs are generally——

Mr. GINGREY. The personnel involved in the research?

Dr. COLLINS. Exactly. The average grant that we give out supports seven jobs.

Mr. GINGREY. Well, the reason I ask that question, I spent 6 years on the House Armed Services Committee and was a strong, strong advocate for the F–22 Raptor. Now, it happened to be finally assembled in my Congressional district and it involved at least 2,000 jobs, and whenever I advocated on behalf of that program, I think I was rightly challenged to justify my support based on air superiority and the defense of the country and not just jobs that would be created in my Congressional district. And again, I think it is the same thing in regard to this and that is why we ask these questions. We all love to see our great research universities like in Georgia, I will mention Georgia Tech first because that is where I went to school, but the University of Georgia as well and the Medical College of Georgia and my hometown of Augusta, Georgia, all these institutions are absolutely fantastic and have great research programs and I hope to see them continue to utilize NIH grants in a way that will foster hopefully the cure of diseases like Alzheimer's and, you know, maybe this business as you mentioned beta amyloid plaque prevention by vaccination. I think that is very exciting.

I know you have got a huge challenge, Dr. Collins, and we wish you well and the wellness of the country of course is dependent on the research that is being done directed by you and these 27 insti-

tutions in NIH. So we thank you for being here, and I will yield back my time, Madam Chairman.

Ms. DEGETTE. The Chair recognizes herself.

Dr. Collins, it has been almost a year now since the NIH approved the final guidelines for human embryonic stem cell research. What is the status of the embryonic stem cell research being funded by the NIH?

Dr. COLLINS. Well, I am happy to say that has resulted in a significant set of advances in terms of both stem cell lines that are available now for federally funded researchers and for new projects that NIH has funded with that new capability that the President's executive order has made possible, and in fact, as of now there are 73 human embryonic stem cell lines that have gone through our very careful process to make sure that they have been collected with the most stringent kind of ethics involved in the informed consent and are now available for federally funded researchers to use, and they are all listed on the registry that NIH has put up for investigators to look at.

Ms. DEGETTE. Are there additional cell lines that are waiting for approval, Doctor?

Dr. COLLINS. There are more than 100 other lines that either already have their applications complete and they are in the process of being reviewed or have started the application process and the investigator who is going to submit has not quite finished supplying all of the data. So this number is going to continue to grow in a very gratifying way.

Ms. DEGETTE. And what is the budget, the NIH budget being spent right now in stem cell research?

Dr. COLLINS. So for fiscal year 2009, in terms of human embryonic stem cell research, the total comes to $148 million—I am sorry—$119 million, and that does not include some additional ARRA funds, a total then for ARRA funds in human embryonic stem cell research of another $22.5 million.

Ms. DEGETTE. So that was in fiscal year 2009?

Dr. COLLINS. Right.

Ms. DEGETTE. Has that increased in——

Dr. COLLINS. In fiscal year 2010, which we of course are still in the middle of so I can't give you exact numbers but I believe that is going to be higher because we have had a lot of new applications as a result of the availability of these new lines.

Ms. DEGETTE. OK. Do you think that the scientific community would benefit from knowing that the ability to conduct this type of human embryonic stem cell research would be codified versus just contained in an executive order?

Dr. COLLINS. So I appreciate the question. I think the executive order has provided the scientific community with a great deal of excitement in terms of the ability to begin to do experiments that were previously not allowable. Whether that would be further increased in terms of confidence about the future by having this codified in legislation is not something I am probably in a good position to be able to comment upon but I understand——

Ms. DEGETTE. Let me ask you this question then, because what I hear from a lot of the researchers is oftentimes these research

projects because they are basic scientific research take a number of years to complete. Would that be correct, to your knowledge?

Dr. COLLINS. Yes, and researchers would certainly like to be confident that their particular experimental approach can go forward without risks of somehow being no longer allowable.

Ms. DEGETTE. I mean, some of these projects people tell me can take 5, 6 even more years to complete.

Dr. COLLINS. Science is a marathon, not a 100-yard dash. You are quite right.

Ms. DEGETTE. Yes. OK. And I also want to ask you, in November 2007 scientists were able to successfully revert human adult skin cells into an embryonic-like state because they inserted a retrovirus. Those resulting cell lines, as you well know, are called induced pluripotent stem cells, or iPS cells. I would like you to tell me about what progress has been made in the iPS research and is this something that the NIH is also funding?

Dr. COLLINS. Absolutely. I have to tell you, Congresswoman, when I read Shinya Yamanaka's paper in 2007 describing how he had been able to take a skin cell and by adding just four genes to it cause it to essentially go back in time and become pluripotent, the hair stood up on the back of my neck. It was one of those moments where you realize this is a publication that changes everything. Who knew it was going to be that possible? So yes, the potential here because you could then produce pluripotent cells from any of us that would therefore be possible to use in the future for therapeutic purposes without rejection.

Ms. DEGETTE. Because they would be a genetic match?

Dr. COLLINS. It would be a match.

Ms. DEGETTE. Now, to date, let me ask you this. To your knowledge, Dr. Collins, have the iPS cells substituted for the embryonic stem cells? Because that is the press accounts that we have seen that now we don't need embryonic stem cell research anymore.

Dr. COLLINS. They have not. I think we are still trying to understand what is the same and what is different between a human embryonic stem cell, which is the gold standard for pluripotency, and the iPS cell, which has a lot of the same properties, but if you look very closely by some of the measures that can be done about things like epigenetics, DNA methylation and so on, it is clear that an iPS cell is not identical to an embryonic stem cell.

Ms. DEGETTE. And in fact, a lot of the researchers have told me—I am a layperson so that is why I asked—is that in fact all these types of stem cell research when done ethically are important to support because the researchers can use all of them to sort of help validate the other research and to help in the lab.

Dr. COLLINS. I believe that those who are studying iPS cells are pretty much all committed to doing side-by-side comparisons to human embryonic stem cells to see what the similarities and the differences are, and that comparison continues to be really important.

Ms. DEGETTE. That is what the researchers tell me too.

I want to talk to you for just a moment about the recent regulations that the NIH has developed on the conflicts of interest because many of us were on this committee in 2004 when we conducted our last investigation of the conflicts of interest at the NIH

with your predecessor, and I know that you have got draft guidelines out for comment. My question, we sort of had thought we had solved this problem several years ago, and I know Dr. Zerhouni was quite committed to solving it. What do these new draft regulations contain that are not in the regulations that were promulgated a few ago and do we think this is going to help solve some of the very real conflicts of interest that we are seeing with researchers?

Dr. COLLINS. So the discussion that you had with Dr. Zerhouni a few ago was largely focused on investigators who were NIH employees who worked in the intramural program of the National Institutes of Health, and there were some egregious examples of conflict of interest that came to light. The consequence of that was to tighten those rules up very significantly and they remain, I would say, above reproach in terms of the way in which those have limited any kind of bad behavior. What has not been taken on at that time, though, was to consider all of those grantees out in universities across the country who are not NIH employees, they are employees of universities, and NIH therefore has a different relationship, but recognizing that there were examples there as well where investigators who were NIH grantees were not disclosing that they were supposed their financial conflicts. NIH has now stepped forward to require institutions to take a much more heavy hand here in terms of checking out whether their investigators are engaged in conflicts of interest, and there are several proposals here as part of the NPRM that we are now seeking comment on that would require a much more extensive disclosure of any kind of financial conflicts that investigators might have including posting those on a public Web site so that it is possible for anyone to see what is going on and not have this being done behind a curtain. This also requires the institutions to have a much clearer plan about how they are going to review and notify NIH about those financial conflicts. Again, we are seeking comments on those over the course of the next month. There has been this recent observation that in one instance an investigator left one university and was able to escape sanctions on that basis and we are now considering what could be done to prevent that in the future as well. So there is a lot that we can do here, although we are to some extent limited in that our relationship is primarily with the institution and not with the investigator.

Ms. DEGETTE. But if you required the institution to make disclosure, then that burden would be on them.

Dr. COLLINS. Indeed, and that is the goal of the NPRM.

Ms. DEGETTE. The Chair now will recognize Mr. Whitfield.

Mr. WHITFIELD. Thank you very much, and Dr. Collins, we appreciate you being with us here today very much.

I know that NIH is involved in a lot of projects like the Molecular Library Initiative and your collaboration with FDA, EPA, the National Chemical Genomics Center and others to identify small molecules, their biological behaviors and so forth leading to I guess what we refer to as a big biology or human metabolome project, and I was wondering if you could just give us sort of an update on the money that is being spent on agencies on this and what you view the prospects are for this type of initiatives.

Dr. COLLINS. So I believe this is a very exciting area. This is bringing chemistry and biology together in a new and exciting way and making those resources available to academic investigators. It is another kind of high-throughput science. The idea here is that if you are interested in developing some kind of a compound, an organic molecule that might ultimately become a therapeutic, a drug, you need a way to empower academic investigators to get engaged in that process and not just hope it is going to happen, and that has given us the impetus to put together a series of four of these high-throughput screening centers, and you mentioned one of them, the NIH Chemical Genomics Center, but there are three others. Collectively, we spend about $60 million each year on these centers, but it makes it possible for an academic investigator who has just made a basic science discovery to move into this possible translational application in ways that just weren't happening before. I would like to see us push that really hard right now, because we are in a circumstances where there have been a lot of basic discoveries that are perhaps even more ripe for translational applications than ever before, but many of them are too early for the private sector to necessarily see them as ripe enough for them to take on. If we could come up with a strategy for academic investigators, take it a certain way, de-risk a project, and then hand it off to a private company who would then carry it the rest of the way to approval, that is a pretty good model. Companies like that. We at NIH like that. This may be our path towards the future.

Mr. WHITFIELD. Now, it looks like there would be some real exciting breakthroughs and an opportunity here for partnerships with private entities as well.

Dr. COLLINS. I totally agree, and I think that is a new model that maybe hasn't really been tried to this extent before. Companies would tell you they are also really looking for new models. The development of new therapeutics has not been going all that well for them in the last few years. Here is a way to speed that up.

Mr. WHITFIELD. And I have also been told that some of these new techniques have been used in analyzing the dispersants that they are thinking about using in the Gulf oil spill. Is that correct?

Dr. COLLINS. That is correct, so we have a marriage here between the EPA and the National Institute of Environmental Health Sciences, the National Toxicity Program and this NIH Chemical Genomics Center to try to use the same technologies that are being used to develop drugs to also study toxins.

Mr. WHITFIELD. Well, do you think you could put up with some of us sometime coming out to see the National Chemical Genomics Center?

Dr. COLLINS. We would welcome that, Congressman. Just let me know. We will set you up with quite a tour, and I guarantee you, you will be amazed at the way in which this operation has taken shape with a robot that is capable of screening hundreds of thousands of chemical compounds in just a few hours. It is amazing to see.

Mr. WHITFIELD. And Madam Chairman, I would like to yield the balance of my time to the ranking member, Mr. Shimkus.

Ms. DEGETTE. The gentleman is recognized.

Mr. SHIMKUS. Thank you. I just wanted to follow up in Chairman Emeritus Dingell's comments on the ARRA benefits on the tax credit—not the ARRA but the health care bill. I have been crying and asking for hearings on the health care law since I became ranking member. I am glad he took the opportunity to address the health care law. I do think questions like that could be done in a hearing on the overall law. I just want to put in the record that $27 billion in tax increases to the pharmaceutical companies makes it more difficult for them to do the R&D for new drug development. The 1099 provisions for small companies that require a 1099 form for every $600 cost added will add additional burden to small companies to be able to do that. So where there may be some tax credit help, I think a lot of people would say that the burden on the small pharmaceutical companies are increased under the health care law.

And I will just end on, the iPS system, as my good friend was talking, it may—there may be scientists who want them both to go on but the iPS does evade a very important question that would help unify us versus divide us. It does address some moral ethical problems that many Americans have on embryonic stem cell research, and I yield back.

Ms. DEGETTE. Mrs. Christensen.

Mrs. CHRISTENSEN. Thank you, Madam Chair, and welcome again, Dr. Collins.

As you know, one of the great successes in the health care reform bill was elevating the National Center on Minority and Health Disparity Research to an institute, something that we are very excited about, and all of us who have worked for years in health equity or the elimination of health disparities are really anxious to hear about the role that you envision for this new institute at NIH, so my first question would be, what are your plans to ensure that the new institute will play a pivotal role in helping to ensure and coordinate all research efforts across all of the other institutions and centers so that they would include health disparity elimination variable and measures throughout the entire research design and spectrum?

Dr. COLLINS. So we also were delighted to see that the health care reform bill included this important redesignation of NCMHD now becoming the National Institute for Minority Health and Health Disparities under the direction of Dr. John Ruffin, and this does bring that part of NIH into the same status as the other institutes that direct many other kinds of research. It certainly underlines the critical way in which NCMHD and now NIMHD plays a correlating and organizing role in the entire NIH's agenda for health disparities. That has been going on for some time but this further strengthens the hand that Dr. Ruffin holds, and I think we all welcome that.

This will of course further add to the importance of those rolling 5-year health disparity strategic plans which NIMHD is charged with putting together with input from all of the other institutes. It will take lots of collaboration between the institutes, but I can tell you, having been at NIH now for 17 years, the importance of health disparities and the investments that need to be made there is certainly a shared goal across all of the leadership but it is nice

now to have an institute that stands up in a very visible way to take charge of that.

Mrs. CHRISTENSEN. Well, thank you. In a recent interview, I think it was Science, you spoke of the pressures of year-to-year budgeting and the possible impact of our Nation's current economic situation, but if you had to find, as you said and you alluded to the possibility of it, you find yourself cutting grant budgets or cutting back on some areas of science or have to decide which institutes get the 3.2 percent increase and which don't, I hope that you will consider that the new institute is starting out brand new, is grossly underfunded, so as part of your plan as you implement the Patient Protection and Affordable Care Act to bring its budget in line with the other institutions.

Dr. COLLINS. Of course, I would love to see that happen, and the challenge of course as you probably well know is all of the other stresses that we have on the overall NIH resource total as we face what may be a particularly difficult year in fiscal year 2011, recognizing the economic downturn and the ending of the Recovery Act dollars. We are going to be stressed in all kinds of ways trying to maintain the resources and the environment of the biomedical researchers who are so critical to our future. Estimates are that our success rates in fiscal year 2011 may fall to historic lows across the board, and of course, you can appreciate, I hope, that that makes any special kind of corrections even more difficult than they otherwise would be. We all hope for times where those things will be easier but I don't think that next year is likely to be an easy time.

Mrs. CHRISTENSEN. Well, we don't expect it to be an easy time but they are starting out at such a low budget, and if they are really going to function as an institute, their budget would really have to be greatly increased, and given the extent of the health disparities in racial and ethnic minorities, you know, it really needs to be a priority.

In your testimony, both written and what you gave here today, you talked about diabetes, Alzheimer's, cancer, all of which disproportionately impact African Americans and other racial and ethnic minorities but African Americans in particular, yet there was no mention of the disparities or how NIH would direct research to close those gaps. In that same interview that I read, you talked about a big think that occurred and the outcome of that big think were several areas that may need more focus and attention. Were health disparities one of them, and if not, is there going to be a big think about health disparities?

Dr. COLLINS. I appreciate your question. Yes, it was one of the very significant conversations we had. The big think was a meeting where I brought together about 55 or 60 individuals that I think are able to really look at the entire landscape and give advice about where investments are most needed and most opportune, and certainly one of the groups we had of the three groups focused very much on this general area, what can we do about the health of the Nation and health disparities emerged as a particularly powerful part of that. Reed Tuckson led that particular discussion.

Mrs. CHRISTENSEN. Good.

Dr. COLLINS. And I think we got some strong messages, and of course, the summit that was held a year and a half ago that Dr.

Ruffin organized very much focused on health disparities and itself produced a blueprint of additional needs. The only thing I would want to say, although I would agree, we are not putting enough resources into health disparities, we are not putting enough resources into many other things too, but I hope it is clear that the investments in research on health disparities are not limited to that one institute, that every institute at NIH has an important portfolio in this area, and Dr. Ruffin's job is to be sure that we are coordinating that in a way that we get the maximum benefit from the dollars we are spending.

Mrs. CHRISTENSEN. Right. I am aware that the other institutes and centers are doing research but we want to make sure that he does have that ability to coordinate.

You also said in that interview that we have a lot to do, and this is sort of a quote, at least part of it is a quote, "We have a lot to do to figure out how do people decide about altering behavior." In the case of racial and ethnic disparities or any health issue, behavior is one of the many issues along with environment, access and others that requires research. Does your response where you say "We have a lot to do to figure out how people decide about altering behaviors," does that response mean that we will see a greater emphasis on behavioral research at NIH?

Dr. COLLINS. I think it is timely to focus a lot of attention on behavioral research if we are talking about prevent especially. So much of what we are learning won't do any good if it is not transmitted to people in a way that they understand and if it doesn't motivate health behavior changes whether it is diet or exercise or other activities, and I think you will see—in fact, one of our new initiatives in the Common Fund is called the Science of Behavior Change, how do we learn more about what actually is involved when somebody changes their health behavior, how do we inspire that in circumstances where we have the evidence but we haven't been very good at actually getting the result. You are going to see a lot more of that.

Mrs. CHRISTENSEN. Well, you partly answered one of my other questions about what were you focused on in the Common Fund, but I am going to yield back.

Ms. DEGETTE. Mr. Pitts.

Mr. PITTS. Thank you, Madam Chairman.

Dr. Collins, a recent article in the New York Times claims that the Human Genome Project which you worked on has not yielded many medical benefits. Is that an accurate statement?

Dr. COLLINS. Well, you might not be surprised to hear that I didn't quite go along with Mr. Nicholas Wade's story. Mr. Wade has over the years been a bit of a cynic about genomics, and I think that came through loud and clear. Today's New York Times in a different article by a different reporter has, I think, a much more upbeat and balanced view about the way in which genomics is inspiring new ideas about therapeutics. In sort of responding to Mr. Wade's rant, I sat down for 10 minutes just to see if I could come up in 10 minutes with 25 significant advances in medicine that come out of genomics, and I had no trouble doing so. Somehow they didn't appear in his article.

Mr. PITTS. OK. Thank you. To follow along the line of questioning of the chairwoman, you said that regarding the regulations on conflict of interest that there had been egregious examples of conflict of interest with federal employees. Can you explain the type of example you are talking about?

Dr. COLLINS. Well, I will tell you the one that got attention in the last week, so a psychiatrist who was doing research at Emory University, Dr. Charles Nemeroff, was found to have been receiving large sums of money from pharmaceutical companies that he had not disclosed. Those sums of money were in the same general area as his own research, casting into some question whether his research results were in some way tainted by the receipt of those dollars. When that finally came to light, he admitted that he had been receiving those funds and claimed that he didn't know he had to disclose them. Emory University in consultation with the NIH decided to strip him of his chairmanship and to also remove him as the head of his particular grant. Dr. Nemeroff then actually in the space of a year or so after that sanction moved to a different university, the University of Miami, where because of the current rules, because NIH's arrangements are with institution and not with individuals, Dr. Nemeroff was now able to apply for new grants. He has not received any grant funding from NIH, I am quick to tell you, but he was able to apply, and I think that raised a lot of questions.

Let me say, because I think it is important to put this into the record, that an individual was also involved in a certain way by innuendo in this, Dr. Tom Insel, who is the director of the National Institutes of Mental Health, was in some way implicated by a reporter as not having conducted himself properly. I would really like to defend Dr. Insel in that regard and to say that in his many years of service to the NIH, Dr. Insel has proven to be an exceptional scientific leadership, has led the NIMH with great skill, has encouraged innovative advances in biomedical research. He has been a person of great integrity, a dedicated and visionary public servant, and I am fortunate to have him on my team at NIH.

Mr. PITTS. Thank you.

Let me go a little further in embryonic stem cell research. About, if you can ballpark it, how many years have we been doing research on embryonic stem cell research, how many years in humans, how many years in mice? Can you just ballpark it for us?

Dr. COLLINS. So in mice for quite a few decades. In humans, it was in Madison, Wisconsin, Ms. Baldwin, where Jamie Thompson first developed the human embryonic stem cell.

Mr. PITTS. What year was that?

Dr. COLLINS. That was 1998.

Mr. PITTS. Nineteen ninety-eight?

Dr. COLLINS. Right, so about 12 years.

Mr. PITTS. Have there been any clinical trials using embryonic stem cells that have produced improvement for human patients?

Dr. COLLINS. So there has only been one clinical trial for human embryonic stem cells that have been approved by the FDA, and that is a trial by the company called Geron for spinal cord injury, and they have not yet enrolled the first patient because of safety concerns but are expected to later this year, so it is still early.

Mr. PITTS. OK. What about with adult stem cells? Have there been any clinical trials using adult stem cells that have produced improvement for patients?

Dr. COLLINS. So adult stem cells covers a lot of territory. Certainly stem cells found in the bone marrow have been utilized for a long period of time for bone marrow transplantation and have saved many lives in circumstances where that was an important task. But importantly, those kinds of adult stem cells don't have the same pluripotency that an embryonic stem cell would and so their applications would be limited to certain things and would not be possible, for instance, to use those for all the applications that embryonic stem cells are being contemplated for.

Mr. PITTS. But there have been human protocols developed for human treatment, right, therapy for human patients with adult stem cells that you are aware of?

Dr. COLLINS. Again, bone marrow would be the one where most of those experiments have happened, so that has been very successful in that limited set of applications but would not have been possible to apply for other applications like Parkinson's——

Mr. PITTS. What about with iPS cells?

Dr. COLLINS. IPS cells are a new development as was already raised, very exciting, not yet tried in any human applications. We have just announced the formation of an iPS cell center on the NIH campus to try to speed up those applications for human therapeutic purposes but it will probably be a few more years before we are sure that they are safe because those cells are capable of forming tumors.

Ms. DEGETTE. The gentleman's time is expired. Mr. Murphy.

Mr. MURPHY of Connecticut. Thank you, Madam Chair.

My apologies if you covered this particular piece of this debate already, but I think last week the NIH advisory board authorized three new stem cell lines for research, and I just wanted to ask a broad question on that subject as to how that process of approving new lines is working and if you sort of feel that that process is moving swiftly enough in a sufficient manner.

Dr. COLLINS. So I think it was seven new stem cell lines that were put forward by the advisory committee advising me. I have not formally made the decision but expect to do so in the very near future. That brings to 73 the number of human embryonic stem cell lines that have been approved for use with federal funds.

I think the process is actually working quite well. Basically we ask investigators who have derived the stem cell lines to supply documentation about the nature of the informed consent that was used to obtain those because we want to be absolutely sure that that was done at the highest ethical standards. If they are able to do so in a fashion that is right down the line to every detail consistent with the NIH guidelines, we approve those administratively and we can do that quite quickly once we have all the documents. But some of the stem cell lines were derived years ago and the process of getting consent and the specifics of the details have changed a bit over that time but we have a working group of distinguished bioethicists and biologists who look at those circumstances to try to see whether those particular stem cell lines at least follow the general principles that we would like to see, and

if they agree that they have, then they put those forward for approval as well. They have approved quite a few of those.

Interesting, last week, though, they recommended disapproving a whole set of lines where they thought the consent had a problematic clause in it, which was basically what we call exculpatory language, which according to the common rule really should not be in an informed consent process and they didn't feel if were doing this carefully that we could allow that. That was a bit of a heartache because that was a whole lot of lines that a lot of people were I think hopeful they would get access to but if we have guidelines, if we have ethical standards, we probably need to pay real close attention to them.

Mr. MURPHY of Connecticut. And I appreciate even in the face of some resistance your holding that line. I think the future of this research depends on people believing that there are ethical boundaries and qualifications for this research, and so I think it is to your credit.

To switch topics fairly dramatically, I wanted to go back to something I talked about in my opening statement about the intersection of private and public research. I have got a real interesting company in Cheshire, Connecticut, Alexion Pharmaceuticals, that produces a drug for a rare blood disorder that I won't attempt to butcher the pronunciation of. The drug is called Soliris, and it is an example frankly of a rare instance where a company has been able to commercialize a drug with a fairly limited application, only a couple thousand cases in the United States at a given time. And I guess my question is this. There are a number of different factors that go into your decision on where you place research. Clearly the top of the list is what in the public interest, what are the diseases and conditions that we have the greatest national interest in confronting, but I would assume an element is also what kind of research is most likely to be done in the private sphere and what research is most likely to not be done there and has to be taken up by public funds. So in the context of rare diseases, I guess I would ask for your opinion as to how that calculation plays out with regard to rare diseases and whether we see more companies like this one in Cheshire being able to do this on a private basis or whether we continue to see the need to have a larger public role in that space.

Dr. COLLINS. I think it is going to be a little different for each disease, and I appreciate the question. I think for many rare diseases, the economics just aren't going to be sufficient to inspire a company to make the investment in taking something all the way to therapy if there is not already a pretty good idea on the table, and what academic investigators supported by NIH can now do increasingly is to make that possible.

There is a new program called TRND, which stands for Therapeutics for Rare and Neglected Diseases, funded by the Congress, $24 million this year and $50 million requested next year in the President's budget, which is exactly to try to provide that kind of de-risking opportunity for these rare-disease projects, not to take them away from a company's interest but actually to try to get them far enough along to inspire a company's interest, and we are seeing that happening now. That program has already started five

new pilot projects for rare diseases. One is for a disease called hereditary inclusion body myopathy. Now, who has heard of that? Relatively few people affected, but there is a very promising therapy and it just needs a little push to get to the point where a company like the one in Cheshire might be willing to pick it up. We are trying to do that, and with rare diseases not only they affect real people and you want to do something for those real people but we often learn things from rare diseases that have a broader reach. My own lab, because I have a small research lab at NIH studying an incredibly rare disease called progeria, which is a form of most dramatic aging, and we could only find 30 kids in the world to try on this clinical trial, which is currently underway at an amazingly rapid pace because we just discovered the cause of this a few years. But what we are learning from progeria is turning out to have pretty significant implications for normal aging and maybe that will turn out to be one of the most exciting things that has come along in a long time in terms of understanding the aging process, all by studying this vanishingly rare disease.

Ms. DEGETTE. The gentleman from Texas, Mr. Burgess.

Mr. BURGESS. Thank you, Madam Chair.

Dr. Collins, again, welcome to our committee. Just on the issue of rare and neglected diseases for just a moment, this past week in the New England Journal of Medicine they had an article about the curious case of colchicine, a drug that has been around for 3,000 years, and yet the FDA decided that since we have never studied this maybe someone ought to, so someone did, and they were given exclusive rights for colchicine for 3 years, an additional 7 years under the Orphan Drug Act, so people who suffer with gout, colchicine is a second-line drug of choice, but went from pennies a dose to several dollars a dose. For people with familial Mediterranean fever where colchicine really can be a benefit are now left facing a situation where their costs are going to significantly go up, so would the NIH be interested in proactively funding any of the research on some of these compounds that have been around for a long time to sort of preclude this problem from happening again to some other illness? Again, not many people with familial Mediterranean. The figure they gave the New England Journal of Medicine was 100,000. I don't know whether that is in the country or globally but it is not a large universe of people, but the people who have it are now significantly affected by the activities of the Food and Drug Administration.

Dr. COLLINS. Dr. Burgess, that is a great question. Dr. Daniel Casner at NIH is the world's expert on familial Mediterranean fever, and I know there is a good deal of anxiety about what this is going to do in terms of the costs of taking care of these patients. Exactly, I think this is something that NIH can do. I mentioned this program called TRND, Therapeutics for Rare and Neglected Diseases, and one of its explicit goals is to try to identify compounds that have been out there for a long time and repurpose them for uses for rare diseases where they might actually have considerable benefit but nobody actually tried that, because if you do that, you have ended up with something which may be both inexpensive and actually you are pretty close to the point of being able to ask the FDA to approve it without going through those

long, long steps of developing a totally new compound. It is a great idea. When we are searching for a new compound for a disease that there is no therapy, we always make sure, we check all the available ones that have already been given to patients that we know are safe and once in a while you turn up with something really exciting.

Mr. BURGESS. You famously were interviewed on the Colbert Report, and——

Dr. COLLINS. Yes, it is true.

Mr. BURGESS. —talked about making—attracting more young people to the study of science and the things you could do to make science appealing to young people. I think the term that was used was "to make science sexy." How are you coming in that endeavor?

Dr. COLLINS. Well, maybe you a better judge of that, members, than I am. You may recall that Colbert suggested that if I really wanted to attract scientists into the field that I needed to sort of loosen up a little bit, take your glasses off and shake out your hair, and against my better judgment, I did that on national television. But I am not doing it this afternoon.

So we are really interested, to get serious here, in terms of trying to recruit the best and brightest of the next generation. We were big participants in National Lab Day where we sent a lot of scientists out to high school classrooms to try to make science a little more real and hopefully less geeky than it often appears to be to the next generation. We are hoping to play some role in whatever happens next in terms of beefing up science in K though 12 education because clearly the way science gets taught to a lot of young people isn't very exciting, and it should be. This is the century of science, especially biology. So many opportunities for people that we would love to see them just jump on and come and join us because this is going to be an exciting time beyond any that anybody has experienced before. In the next few years, we are going to learn all this stuff. We are going to figure out how to apply it. What a great career.

Mr. BURGESS. And I know this question has already been asked, but I was out of the room and I just wanted to ask you to address briefly the—well, Dr. Zerhouni came to us right before—your predecessor—right before he left the post and talked about the wondrous things that have happened with the human genome and cracking the genetic code, the single nucleotide polymorphisms where there was just three in 2003 when I started in Congress. There were now, I don't remember how many he said last fall and there were more being discovered literally every week. But there was some disappointment with the clinical applications of sequencing the human genome, so where are we on that?

Dr. COLLINS. Well——

Mr. BURGESS. Is it the brave new world that Dr. Zerhouni talked about or are we on a dead-end street?

Dr. COLLINS. You know, the first of technology says that when you make a major discovery, the anticipation of its immediate effects is always going to be overblown but the anticipation of the long-term effects will generally be underestimated. I think that is going to be true of genomics as well. There were a lot of wild claims made in 2000 about how this is going to change everything

overnight. You and I knew that there was a lot more steps involved from understanding what the letters are in the DNA code to figuring out what to do with them. But I think the advent of personalized medicine is certainly coming along now in a quite gratifying way.

In today's New England Journal, by the way, and I put this at your place, is an article by myself and Peggy Hamburg called "The Path to Personalized Medicine" going through some of these really exciting advances and also making it clear how FDA and NIH are working together to support them. So I think any declaration that the outcome of the genome project has been disappointing is probably just not based upon realistic expectations. I do think that revolution is going to be quite something when it takes full shape in the next 10 years.

Mr. BURGESS. I want to come back to that partnership of NIH and FDA in a minute but before we leave the concept of the human genome, in the interest of full disclosure, I had my genome sequenced and it is a fascinating study, and I actually am glad I did it, but there has been some controversy about the direct-to-consumer marketing of these tests. In fact, our committee, our Subcommittee on Oversight and Investigations, is going to be conducting or is conducting a bipartisan look into that. I guess at this point what I would ask you is, would you be willing to work with our staffs on both the majority and the minority side as we look into this issue? Obviously we want this done correctly. We don't want people hurt or misled by the process, and I think that is what raised the initial concerns when one company was marketing it in a commercial drugstore and then withdrew it, and it raised a lot of questions. You know, there is no question of the value of the procedure.

On the issue of the FDA, I mean you guys got a ton of money in the stimulus bill. I mean, it was almost immeasurable the amount of money you got, and no one ever had seen that much money before even in government. And so you produced—you put it to work and you are producing all this stuff. Now, the FDA as we heard the other day in another subcommittee hearing, it is kind of a little bit like a bottleneck in the pipeline. So how are you and Dr. Hamburg working out these problems between your two institutions?

Dr. COLLINS. So two ways and probably many other smaller ones but two major ways. One is the formation of this NIH/FDA leadership council, which will have senior leadership from both agencies at the table on a regular basis with projects and ideas coming to us both from industry and from the advocacy groups, all the stakeholders, to really try to say where are the bottlenecks, what are we going to do about it, let us get serious here.

The second is to have an actual scientific organizational plan about how are we going to give FDA some additional information about how to do regulatory science because many of the things that are coming at them are new. If you have a clinical trial where everybody in the trial is on a slightly different combination of therapeutics, as will happen soon for cancer where combination therapy is going to be the name of the game with all these various targeted therapies that are possible, how do they review that? We need

science to understand that. That particular regulatory science program is funded jointly by FDA and NIH but actually because FDA is a little strapped on cash, the NIH has come up with a larger proportion of the funds and we are happy to do that, and I am happy to work with a scientist and a physician with the capabilities of Dr. Hamburg. I think we are actually forming a pretty good partnership.

Mr. BURGESS. Can we expect a——

Ms. DEGETTE. The gentleman's time is expired.

Mr. BURGESS [continuing]. Report at some point from you on that? Are you going to be getting back to the committee on that issue?

Dr. COLLINS. I would be happy to do that.

Mr. BURGESS. OK.

Ms. DEGETTE. The Chair will announce that we are expecting a series of three votes on the floor. The Chair will recognize the gentlelady from Florida for questioning, 5 minutes, and then we will recess for the votes. We will return immediately upon the completion of the votes because other members want to question, and if Dr. Collins agrees, if people have additional questions, we may come back for a brief second round.

Dr. COLLINS. I will be happy to be here as long as you like.

Ms. DEGETTE. The gentlelady is recognized.

Ms. CASTOR. Dr. Collins, the Clinical and Translational Sciences Awards are very popular. These awards are focused on translating NIH research into an understanding of health impacts. Does NIH plan to expand the initiative to create more CTSAs nationwide and include additional rounds of funding? I know that there is currently one CTSA in Florida at the University of Florida but the University of Miami has applied several times and has been denied, and the University of South Florida would like to get into that CTSA. They are popular because they include training funding, and there is a concern about where training funding will come from if CTSA grant applications are denied and will applicants still be eligible for training dollars from the National Center for Resources or other institutions under NIH?

Dr. COLLINS. Well, I appreciate your question because the CTSAs are a very important part of NIH's clinical research network and our plans including all kinds of new and innovative approaches to clinical applications, therapeutics, diagnostics and so on. We have currently funded 46 of the CTSAs around the country. It is a very competitive process. There is another round of competition that has just gone on, and there will be a few more announced as a result of that, and then there is one more competition coming next year, but the goal was to fund a total of 60. That pretty much will exhaust the dollars that are possible to put into this, which is now coming close to half a billion dollars for these 60 centers.

We do very much expect that they are going to link up in interesting networks both regionally and nationally so that the whole will be greater than the sum of the parts, and every one of the CTSAs has been encouraged, as your question pointed, to focus on training, to focus on bringing together disciplines that maybe in the past had not talked to each other, even within an institution, but also to building networks around each of the CTSAs of other local

institutions including community hospitals, and community outreach is a big part of this as well.

I wish we could come up with the dollars to fund 100 instead of 60 but 60 is probably as far as we can go. We do expect that out of this will arise a whole new way of approaching clinical research. I have been to visit now four of these and I will go see another one actually tomorrow, the one in St. Louis. It is very interesting. They are all a little different, and they are taking advantage of what they have locally in terms of special expertise to make themselves different, and it is pretty exciting when you see the ways in which they have people talking to each other who never would have been in the same room before, and they are certainly encouraging training in clinical research, which has been a big concern because many physicians have been sort of staying away in droves when it came to research because they had big debts to pay, it wasn't clear what the pathway was, it wasn't clear where they were going to get mentored. The CTSAs are really helping to turn that around. It is going to be a tough process, of course, to turn that around because there are so many other things pulling on physicians, but I think this is going to be a really interesting few years to watch. The first CTSAs are just now coming up for their first renewal because this is a pretty new program. We have high hopes.

Ms. CASTOR. Good. I will look forward to talking with you more about how they evolve.

Training awards are also critical for our medical schools. These awards are relied upon to train medical students in specific disciplines, and most training awards are within discipline-related institutes under NIH, for example, the National Heart, Lung and Blood Institute. I understand that it is increasingly difficult to get training awards. Is this because of a lack of resources and will there be additional T–32, T–35 training grants available and will additional funding be available for career development awards both individual and institution?

Dr. COLLINS. So we certainly believe that training is critical for our future and every one of the institutes has a special way of trying to support that. The National Institute of General Medical Sciences, NIGMS, is a particularly important part of NIH for training organizational efforts and they fund, for instance, the M.D./Ph.D. training programs, the medical scientist training programs, which are a way in which we are hopefully nurturing a particularly energetic and inspired group of future leaders who get both the M.D. and the Ph.D. degree. We have been both concerned about whether we are training enough individuals and whether we are actually supporting them adequately. One of the things that we are trying to do is to catch up on the stipends for trainees, which have been flat for a long time, and we are clearly asking people to remain in training positions. Many of them are already with doctoral degrees and really quite low salaries, and that is beginning to be a problem in terms of recruiting people to do this, and we are going to try to pick up a little bit on that.

Again, resources. I keep coming back to that with many of the questions with the fact that we are facing potentially a very difficult time in fiscal year 2011 and perhaps beyond. We would love to expand training programs but where would we take the dollars

from in order to do this with so many other needs for disease research, for grants and so on. We are every day trying to figure out how to get that balance right.

Ms. CASTOR. Thank you.

Ms. DEGETTE. The committee will be in recess until the completion of the third vote.

[Recess.]

Ms. DEGETTE. The committee will come to order, and the Chair recognizes Mr. Space.

Mr. SPACE. Madam Chair, if I could, I don't expect to exceed the 5 minutes but I did not do an opening statement today, if I could be permitted the luxury of 8 minutes?

Ms. DEGETTE. Yes, you are recognized for 8 minutes.

Mr. SPACE. Thank you, Madam Chair.

Thank you, Dr. Collins, for joining us today, and for offering your testimony and for the work you do at NIH. I personally think it is an underappreciated agency that we should be devoting more resources and assets toward.

I wanted to focus my questions today, however, on one specific disease, and that is diabetes. As you probably know, the ADA recently conducted a comprehensive study in which it was determined that—these are 2007 numbers, by the way, which undoubtedly are significantly lower than they would be today, but they determined that we are spending as a Nation about $174 billion every year. Most of that money represents costs associated with health care for those suffering from diabetes and particularly those in the chronic stages, but a significant portion also represents lost productivity, and this is one disease in one year we spend more as a Nation than we did, for example, in just about any year during the war in Iraq. Obviously if we were to be able to cure this disease, we would mitigate and in fact eliminate the expenditure of trillions of dollars over the next 50 years in terms of the long picture.

I happen to have a son who suffers from type 1 diabetes. He is 19 now. His name is Nick, and he was diagnosed when he was 6 years of age, and after his diagnosis my wife and I, we knew very little about diabetes at the time but we began to educate ourselves on this devastating disease, and this was in 1996. Here we are 14 years later. In 1996, it was my impression that we were 10 years away from a cure, and this was based on exhaustive studies and research that I committed myself because of an obvious personal interest, and here we are 14 years later and I am still hearing the same thing, we may be 10 years away from a cure. And I am familiar with the closed loop system and the concept of an artificial pancreas, that if every type 1 diabetic in the country had it would eliminate countless episodes of suffering, premature death and disability but it would also end up saving a lot of money in the long run.

And my question to you is regarding the special diabetes program. I understand that this has been funded at $150 million per year. Incidentally, it sounds like a big number, it is a big number, but if we are spending $174 billion a year combating this disease and when you take 10 percent of that figure and spread it out over 5 years, say, $17 billion, just round it downwards to $15 billion, if we spend $3 billion a year over 5 years, my opinion is, we could

give every type 1 diabetic in the United States a closed loop system that worked and that was reliable and would more than pay for itself in a few short years. My question to you, Dr. Collins, is, what is your assessment of the special diabetes program, its importance to researching and developing advanced methods of treatment, maintenance and possible cure when it comes to type 1 diabetes?

Dr. COLLINS. Mr. Space, I appreciate your question, and especially the personal experience you have had with your son Nick, and I think parents who have had that experience must be like you, frustrated that we don't yet have a better solution to this clearly important and very serious disease of type 1 diabetes. The special diabetes program, which, as you point out, is $150 million a year, it is set to expire at the end of fiscal year 2011, and I know there are some anxieties amongst the investigators working in those projects about whether they are going to have to phase out their efforts at that point. It certainly includes a number of, I think, rather ambitious efforts, and certainly the artificial pancreas is one of those dreams that we all hope will come true in a broader sense in the not-too-distant future but obviously many challenges there in terms of how you get the engineering and the biology right so that you have a system that is reliable, because obviously any system that has the capability of delivering insulin needs to be failsafe because overdoses would be potentially very serious. I think there is real progress being made there but I am sure from your perspective and from mine, it is slower than we wish it could be.

In terms of type 1 diabetes and what causes it in the first place, we have I think a much better idea of what the genetic factors are. We now have accounted for more than half of the heritability of type 1 diabetes, and there is this program called TEDDY which is now following several thousand children who are at high genetic risk to see whether in fact they begin to show some signs of the autoimmune component, which is the sign that the disease is getting started because as you probably know, by the time a young person shows up with actual symptoms of diabetes, most of those beta cells in their pancreas have already been destroyed by the autoimmune process and the best hope is to catch that early and then treat it with appropriate drug therapies including a new therapy called rituximab.

So I would say there is reason to be optimistic that the steps are moving forward but I hear what you are saying, that you heard that in 1996. I am impatient too. I want to see this disease conquered. I want to see the best ideas supported to make that come true. It is challenging to figure out for us exactly how to take the resources we have got and apply them in the best way. We do what we can in terms of estimating what is going to work or what is not going to work. There are steps forward. Sometimes there are setbacks, especially in clinical research where you know you have to come up with something that is both effective and safe, but I think with the way that the field is moving, and it is hard for me to see that that dream you were promised in 1996 is not going to happen. It is very hard to put timetables on these kinds of trajectories. I wish I could.

Mr. SPACE. Apart from the obvious benefits associated with the alleviation of human suffering and saving lives, is it your assessment that that would also save a lot of money?

Dr. COLLINS. A lot of money, absolutely, and I certainly hear what you are saying both for type 1 and for type 2 diabetes the huge sums of money that we are in our medical care system are going to take care of individuals. We also have very vigorous research programs on type 2 diabetes, particularly now in prevention where we have the ability perhaps for people who are starting to tip over into that to be able to prevent the full onset of the disease, following up on the results of the diabetes prevention program, which has taught us how to do that with simple things like diet and exercise and lifestyle changes that can be successful if properly managed.

Mr. SPACE. And just finally, in the event that the special diabetes program were not to be reauthorized, would that have a deleterious or negative effect on advances in he field?

Dr. COLLINS. It certainly would. I mean, with all the momentum that has been generated because of that special program, the idea that those dollars would sort of come to a halt would force the NIDDK, the diabetes institute, to make some very difficult decisions about what they could continue and what they could not.

Mr. SPACE. Thank you very much, Dr. Collins.

Ms. DEGETTE. Mr. Space, the Chair will announce that we have for—the Diabetes Caucus has asked for a full hearing on NIH efforts towards diabetes research and prevention and so we will look forward to that hopefully later this year.

Mr. SPACE. And I look forward to that as well, Madam Chairman.

Ms. DEGETTE. The Chair recognizes the gentlelady from Wisconsin, Ms. Baldwin.

Ms. BALDWIN. Thank you, Madam Chair. I have ambitious plans with my 5 minutes of questions but we will see how far I get into this.

First I just wanted to make a comment. I was present when Dr. Christensen was talking, asking questions and bringing all of our attention to the issue of health disparities in minority populations, and I just wanted to share with you my interest in expanding the way we think of that to include also the lesbian, gay, bisexual and transgender population. In years past when we have had predecessor in front of the subcommittee or other agency heads, I have asked about the state of knowledge on LGBT health and what sort of data collection we have, what sort of information, and I am sad to say that the answer was, you know, either we will get back to you or we are not aware of anyone even asking questions related to sexual orientation or gender identity to be able to gather the evidence and the data. I don't know what role you might have personally played in the focus that the IOM is now putting on this question but I am delighted and want to commend any role that you did play in bringing that together because I think it will examine the current state of knowledge and hopefully produce recommendations of where we can obtain even greater knowledge. So that is just a comment.

Really, with the rest of my time I wanted to get as much of a status update on some new programs, et cetera. If you don't have the information available today, please feel free to respond at a later point. But last year the Christopher and Dana Reeve Paralysis Act was signed into law. I had authored the freestanding bill before it was included in the public lands bill. And this authorized NIH to undertake two grant-making processes. One would fund grants for consortia in paralysis research, and the other would grant funds to maintain a clinical trial network with sites focusing on people living with paralysis. I am wondering if you can give me any update on the implementation of this new legislation.

Dr. COLLINS. I would be happy to. Very quickly, in terms of LGBT, we are in fact supporting and we have done an inventory here some 272 projects through NIH research costing over $239 million, so there is a research portfolio there. But we are very much looking forward to the results of this IOM study, which I strongly support, to try to learn more about the needs and the research opportunities that NIH should be addressing.

In terms of the Christopher and Dana Reeve Paralysis Act, yes, there certainly has been as a consequence of that the formation of a network here which is funded by the National Center for Medical Rehabilitation Research, which is within the Child Health Institute. Traditionally that is where rehabilitation research has been located. But together with the Neurology Institute and the National Institute for Bioimaging and Biotechnology, that resulted in solicitation of a whole bunch of interesting proposals and in fact seven sites that received the best peer review recommendations are now being funded by those three institutes, and they are going to look at biological, medical, behavioral, social aspects of paralysis and very much try to make this a consortium effort as opposed to a collection of disconnected research projects.

Ms. BALDWIN. Great. Thank you. Recovery and Reinvestment Act funds were awarded through the National Center for Research Resources to address the critical research infrastructure needs across the Nation but I would say that the funds were inadequate to meet all the critical needs that are out there, and so I am wondering moving forward, once the recovery dollars are expended, will funds for construction or remodeling of facilities be a priority and be allocated to NCRR?

Dr. COLLINS. So yes, we were delighted in the Recovery Act to have a billion dollars to put forward for construction and renovation, and those grants were rigorously reviewed and fairly recently decisions made and announcements put forward and those $1 billion is going to support grants and new construction in 146 projects in 44 States and the District of Columbia, so this was clearly one of those occasions where dollars from the Recovery Act were going to support both medical institutions and the economy in terms of the reconstruction efforts. Future funding is not included in the President's budget for fiscal year 2011, and I must tell you that when budgets are tight, as we fear they may in fiscal year 2011 and beyond, dollars for this kind of application are often hard to come by, and that is something that Congress decides, we don't decide. If we don't have an allocation in that part of our budget, we

are not allowed to spend the money on buildings and facilities so we wait to see what the appropriators tell us.

Ms. BALDWIN. I see I have run out of time. So I will conclude. Thank you.

Ms. DEGETTE. If the gentlelady has a couple more questions, we had said we would be willing to do a second round, so you can——

Ms. BALDWIN. Oh, I would be delighted to use just a couple more minutes and then I won't need a second round.

The University of Wisconsin has long been responsible for running the National Stem Cell Bank. This year we have been informed that NIH would like to take this process through a competitive rebid, and I wonder if you can tell me a little bit about what the timeline and the selection criteria will be for the rebidding of the National Stem Cell Bank.

Dr. COLLINS. So the University of Wisconsin has been such an important leader in this whole field. I think I mentioned earlier the contributions of Jamie Thompson and the way in which the Wisconsin effort led to the formation of this bank was certainly an important resource for individuals who would want to get access to these stem cell lines and knew that they had been properly maintained and they could count on their quality. Now that there are, as I mentioned earlier in this hearing, 73 such lines that have been approved and going up, we are going into the hundreds before long, there is a big question mark in many people's minds about exactly what is the right way to make sure the lines are accessible to investigators who want to use them. Some of them will probably be used more than others. There will be some favorites, no doubt, as has been the case in the past.

What we are trying to ascertain is whether it is actually time for this kind of banking activity to move into a competitive private sector enterprise because certainly in other circumstances where there are biological resources that many individuals are interested in, the time sometimes arrives where it is more efficient and more cost-effective to have this conducted by a small company who would then be basically recovering their costs of distribution by a modest chart. What we don't want to do, however, is to have that end up resulting in excessive cost for NIH investigators. That would sort of defeat the purpose.

So we are still exploring what the right pathway might be but it seems likely that we will want to set up a circumstances where there is more than one bank, because obviously you wouldn't want to have the entire field resting upon a single resource, and it will be, I think, a few more months before we have a clear sense of what is the best strategy for making sure that we have cell lines that are maintained at high quality and made available to investigators at reasonable cost.

Ms. BALDWIN. I have two more topics. In the fiscal year 2010 appropriations bill, Congress called on the Office of the Director to engage in specific efforts to improve research on women's pain including coordination of a trans-institute research initiative in fiscal year 2010 that will support studies aimed at identifying common etiological pathways and with the goal of identifying potential therapeutic targets, and secondly, a conference to be held along the

same lines. Could you tell me about the status of your efforts in this area?

Dr. COLLINS. So we certainly read that part of the health care reform bill carefully and we are happy to be called upon to work in this area of pain, which we agree is extremely important. There is a pain consortium at NIH which has been in place for several years which involves quite a number of the institutes that have an investment and an interest in this area, and this is another sort of encouragement for that effort to get even more involved. We are in fact planning the conference that is being asked for, which I think is to be hosted by the Secretary in the not-too-distant future because I think there was a timeline on that, and there is also an exhortation in the Affordable Care Act bill about coming up with some new Common Fund ideas for pain research which is certainly something that is being looked at by the pain consortium to see if there are opportunities there.

In addition, there have been a number of specific workshops focused on particular subsets of pain to try to bring investigators together with new ideas, and I must say there are some exciting things coming along. I will just mention one, which is another example of how a rare disease can really lead you to a very interesting new hypothesis. There are rare individuals who are born with what is called congenital insensitivity to pain. There was a particularly dramatic publication a year or so again studying a Pakistani family where a number of the siblings were completely unable to feel pain, which is not actually good for you. These siblings end up involved in street theater where they would walk on hot coals or they would actually pass knives through their arms, obviously amazing people going by, not feeling pain but of course putting themselves in great jeopardy. The cause for that has been discovered and they are basically missing one of these sodium channels that normally transmits the pain signal in the nervous system, and they are otherwise entirely well. Now, that is a really interesting finding and that says if you can identify a drug, a small molecule that blocked that activity and the rest of us transiently, that would be an incredibly powerful pain reliever, an analgesic, and many companies have now jumped on that description of a very rare family thinking this might be the best clue we have in a long time for a totally new approach to pain management.

Ms. BALDWIN. Very interesting.

My last question, and you have been very tolerant of my battery of different updates, I am curious about the National Research Service award funding program. Are there any efforts underway to reframe that, change the amount or the allocation or training funds under that program?

Dr. COLLINS. So we are aware that stipends for NRSA trainees, the Ruth Kirschstein NRSA awards, have fallen behind over the course of many years without having a substantive increase in quite a long time and so we have supported a 6 percent increase in the current circumstance to try to make up some part of that and there has been a sense of the Congress and we agree with this that we should continue to try to catch up a big here. We depend on these trainees to do a lot of the front-line research. It is part of their training, but they are also really important for the produc-

tivity of the enterprise. We certainly wouldn't want talented minds to go elsewhere because they just couldn't figure out how they are going to buy groceries, so we are doing what we can to try to catch up on that, recognizing that we have fallen behind.

It of course comes at a tough time if we are seeing a more stringent budget looming in the future. If we are going to increase stipends, we may have to decrease the number of trainees because there has got to be an ultimate reckoning, and we would hate to do that too so it is just more example of the tough decisions that may be facing us at a time where the economy is struggling.

Ms. DEGETTE. The gentleman from New York, Mr. Engel, is recognized.

Mr. ENGEL. Thank you, Madam Chair.

Doctor, before I came here, I was at my other subcommittee on the Energy and Commerce Committee, which is the Energy Subcommittee, and we were questioning the BP executives and some of the other executives, and I can tell you this subcommittee is much more friendly today.

Dr. COLLINS. Yes, I am glad I am at this time and not in that other room.

Mr. ENGEL. I want to first of all personally thank you for the good work that you do. I followed your work and I am very impressed. You spoke at the New Dems several weeks ago, I was there and very, very impressed with what you had to say, so thank you, first of all, for all the good work that you do.

At that meeting with the New Dems, you had mentioned a drug called, I think it was Iressa, about breast cancer. I am wondering if you could just again tell us about that, and if somebody would want to sign up for it or anything like that, is that possible?

Dr. COLLINS. There are certainly trials going on, so Iressa for which the generic name is gefitinib, is one of these new targeted therapies for cancer about which there is a great deal of excitement, so Iressa basically works by blocking the action of a particular kinase, which is an enzyme that is normally present in cells but in cancer cells from some tumors gets overly activated by a mutation, and if you are somebody who has a cancer that has that specific mutation, Iressa can be extremely effective. I think I told the story of a woman whose cancer was diagnosed—well, she had lung cancer which was already metastatic to her brain in 2002 and expected to live for a few months. She is doing fine today, I am happy to tell you, because this drug was the perfect antidote to her particular tumor mutation.

Now, that is the good news. The troubling part of this is that Iressa doesn't work for about 85 percent of people with lung cancer because they don't have that mutation. They have some other way that their cells have gone haywire and are causing the cancer in their system, but it does say that we are reaching the point with Iressa, with the drug I talked about in my opening statement which is another example of this sort of targeted therapy for cancer where you can sample a tumor and say oK, what is here and then look at your list of drugs that are available and do the match. As that match gets more and more possible because the list of drugs and the lists of targets gets longer, we are going to see a real transformation in the way that cancer is approached, and that is a great

thing but it is personalized therapy we are talking about now instead of giving everybody the same does of chemotherapy.

Mr. ENGEL. Thank you. I would like to ask you a question on gestational diabetes. According to the American Diabetes Association, gestational diabetes affects 2 to 5 percent of all pregnant women, and that is 135,000 cases every year in the United States, and it occurs, I am told, in pregnant women who have never had diabetes before but develop it between the 24th and 28th week of pregnancy, and while it generally goes away after pregnancy, it can have health impacts for both the mother and the baby. I am told that there is currently an insufficient system for monitoring cases of gestational diabetes to uncover trends and target at-risk populations, and for that reason, I and Dr. Burgess have introduced the Gestational Diabetes Act of 2010, and I am wondering if you could discuss some of the research currently underway to address the need for comprehensive information on the causes and best treatment of gestational diabetes.

Dr. COLLINS. It is a very important problem and one that we need to address both in terms of research and in terms of just the public health and trying to identify individuals who have risks of this sort. Gestational diabetes is in fact a risk to the pregnancy as well. It is associated with higher birth weight with prematurity and certainly something that you want to try to control because the mother who has out-of-control gestational diabetes is also likely to end up with preeclampsia. But more than that, if you get the mother through this experience, and most do, the risks that that woman will go on to full-blown diabetes are substantially increased and ultimately about half of women who have gestational diabetes will ultimately become diabetic.

So it is apparently one of those circumstances where pregnancy is kind of a stress on the system, and somebody who may already be predisposed, it becomes more clear in the course of a pregnancy that that is the case. So we need both better methods to monitor during pregnancy, which means our medical care system needs to be of course accessible to those who need those services. It is not particularly difficult to assess this if that person is getting adequate prenatal care, and we need, of course, methods to prevent it in the first place, and it appears at the present time that the risk factors for gestational diabetes are pretty much the same as the risk factors for type 2 diabetes in general, which is to say family history, which is to say body mass index, obesity and exercise, and what we have learned in terms of how to take people who are predisposed to diabetes and prevent that from things like the diabetes prevention program are probably very applicable here as well. But certainly women who have gone through this experience and had gestational diabetes ought to have a particularly good opportunity to recognize the risks to their future health and to be given the same kinds of interventions that we now offer to people with prediabetes to try to reduce the risk of coming down with the disease. So there is a lot we can do there, but I agree, that has not been fully realized.

Mr. ENGEL. I would like to ask you about Charcot-Marie-Tooth disease. There is an innovative partnership between the NIH's National Chemical Genomics Center and the Charcot-Marie-Tooth As-

sociation. I have worked with that association, and I think that this could serve as a model of future rare-disease research and drug development, so am wondering if you could describe the program and offer your thoughts on it.

Dr. COLLINS. I appreciate the question because I do agree, this is a very exciting program. My father-in-law has Charcot-Marie-Tooth disease, so this is a disorder that is not only something from my clinic but also from my family experience. And this is an interesting disorder which causes a weakness of the legs particularly but also the hands over the course of time, and can be quite debilitating, but it is well understood now what the cause of that is, the genetic abnormality has been now laid out in great clarity, but what could you do about it. So working with the NIH Chemical Genomics Center, which is a remarkable facility that has been mentioned already at least once in this hearing, an effort is being made to identify a small molecule, which is sort of a drug that would basically compensate for the genetic problem that is found in individuals with this type of Charcot-Marie-Tooth disease, so called CMT 1A, and that is an early-stage effort but it is a good example of this therapeutics for rare and neglected diseases effort that NIH is putting increasing effort into.

Charcot-Marie-Tooth is too rare for companies to generally see this as a good investment for them in terms of developing a therapeutic but with the Chemical Genomics Center working with academic investigators who know a lot about the disease, if they can push this forward to the point of identifying a promising compound, then you could imagine a company getting pretty interested in licensing that out and carrying it all the way through to a clinical trial.

Mr. ENGEL. Thank you. With the Chair's indulgence, I would like to ask you about mental health problems of children and adolescents, because in my district, we have the Nathan Klein Institute and it is an internationally known psychiatric research facility, and they believe that the unmet mental health problems of children and adolescents is one of the most important continuing problems that haven't yet been adequately addressed, and the research funded by NIH establishes that 50 percent of all mental disorders begin in pediatric ages and 75 percent onset by age 24, and yet as of 2 years ago only about 8 percent of the budget of the NIMH was dedicated to addressing the needs of children and adolescents. So let me ask you this. How does research of pediatric and adolescent mental health issues fit into the themes of opportunity you have identified within your first year?

Dr. COLLINS. Well, I agree with you. Those are critical issues because certainly the onset of a mental health problem in childhood or adolescence means that that individual if not properly diagnosed and treated is going to have a very long course. One of the things that I think we are trying to understand is, what are the advantages of early diagnosis and intervention. I think there is a lot of need also just to understand in terms of basic neuroscience what is going on in the brain in bipolar disorder, in schizophrenia, in major depression and a number of the other conditions that do tend to come on in adolescence. The Human Connectome Project is an effort to try to do that in a more systematic way, putting together

genetic variations with what the linkages are in the brain between various regions and how those neurological tracks are different in people who develop one of these diseases.

But I hear what you are saying about the need to focus particularly on early onset risks, and here I think the National Institute for Child Health and Human Development working with NIMH, which has been the main source of mental health research, and also with the neurology institute, NINDS, is undertaking, I think, a pretty important effort to try to develop a better understanding of normal brain development in young people and then also to apply that to trying to see what happens in the course of the development of one of these diseases. Certainly the National Children's Study when it gets fully up and going will also have the chance to look for very early influences on mental illness in terms of environmental exposures, genetics, et cetera, because we have not really had a very good database and that study which will study now 100,000 individuals from preconception until they age 21 should provide some other important clues.

Mr. ENGEL. Let me ask the indulgence of the Chair. I have another question. Could I—one more question.

Let me ask you about HIV and AIDS research because I think that is really important, and 56,000 people every year are living in the United States become newly infected with HIV, and in your opening statement you mentioned the many ways that NIH research has contributed to the information that we know and the increased life expectancy for HIV-infected people. We had discussed previously an innovative program in the Bronx where I am from. Can you discuss that program and also the current state of HIV/AIDS research, specifically at the community level that NIH is conducting?

Dr. COLLINS. So the program you are referring to is an innovative idea about testing and treating and then linking to care. Let me explain what this is and why it seems to be potentially very beneficial. You are right, 56,000 new cases each year, and that has been pretty flat for the past few years. We are clearly not successful in reducing the new cases of this epidemic, even though we have developed effective antiretroviral therapy and individuals who are HIV positive can now expect to live many decades. Still, we should be doing better in terms of ending the epidemic.

The idea here is that most of the new cases of HIV or many of them, anyway, are actually acquired from individuals who do not know that they are HIV positive because at the present time many individuals do not get diagnosed until they have already developed some symptoms, they are found to have their immune systems already compromised. At least by mathematical modeling and by some small studies done in other parts of the world, it looks as if you tested every one of us every year to see who is HIV positive, and as soon as somebody turned up positive began treating them then, you would both improve their likelihood of a good outcome but importantly you would drop their viral load substantially so that their likelihood of passing the virus on would go way down. So the idea here is that you essentially reduce the viral load of the whole population by identifying infected individuals as early a time as you could and mathematically it looks as if that could actually

end the epidemic without having come up with a vaccine, which has obviously been an enormously frustrating circumstance. To test that, this test and treat link to cure, TLC effort—link to care—has been piloted just recently in the Bronx and here in Washington, D.C., with support from the National Institute of Allergy and Infectious Disease so that we are going to be able to see does this work, not in a mathematical model but in the real world, and we kind of thought Washington, D.C., was the real world and we thought the Bronx was too.

Mr. ENGEL. I do too. It is one of my favorite places. Thank you very much.

Thank you, Madam Chair.

Ms. DEGETTE. Dr. Collins, I would like to ask you one question on behalf of Chairman Waxman, who had other obligations. He is concerned about the peer review process and also the Cures Acceleration Network. As you know, the NIH Reform Act of 2006 required that all research that the NIH conducts or supports has to go through a peer review process, and you pointed out in your testimony that the process is critical to ensuring that federal dollars are spent on the highest quality research. The health care reform legislation that the President recently signed into law established this Cures Acceleration Network, whose goal is to further research into treatments for certain kinds of conditions, specifically the ones we talked about earlier that have few existing therapies. The legislation established a competitive process for reviewing these CAN proposals but it didn't specifically require that grants go through the NIH peer review process, and so it is Chairman Waxman's understanding that the authors of the provision do not intend for the grant proposals to be subject to the process. What is your understanding of how CAN grant proposals are going to be reviewed by the NIH?

Dr. COLLINS. We depend on peer review for everything we do, and the way in which we would expect this program to go forward would be to invite projects that see ripe for investments of this sort which is moving them through the so-called valley of death where you have a promising compound but you want to get it all the way to a clinical trial. Those would have to be peer reviewed to see where in fact are the most promising projects, the most promising opportunities. This is high-risk, potentially high-failure science, but we at NIH are very motivated to push this forward, and the Cures Acceleration Network would provide us with some flexibilities that we haven't really had before. But it would be done with peer review.

One thing I want to say is that the bill does offer some DARPA flexibilities to NIH, so-called other transaction authorities, which we would welcome in that once a project has been peer reviewed and initiated, it gives the project manager some flexibilities about how to move the project forward and to kill a project if it looks like it is failing and missing milestones. So we do embrace that kind of flexibility but I want to assure Mr. Waxman that we would not imagine having projects get into this pipeline without that kind of rigorous peer review.

Ms. DEGETTE. Thank you, very much.

Mr. SHIMKUS. Madam Chairman.

Ms. DEGETTE. Mr. Shimkus.

Mr. SHIMKUS. Just to remind you of the importance of having a hearing on the health care law. It is not a bill, it is a law, and so we need to deal with it, so I am glad that Chairman Waxman thinks that there are some questions that need cleared up based upon the law.

And also, you promised a great litany of things that we are doing and dollars spent. My opening questions dealt with this driving research thing that you are doing, $250,000. You said you would come back and give some answers on that. I would hope you would, because then it is tough for us to defend the good when we have questionable dollars going into questionable directions that we need more clarification on. So thank you, Madam Chairman.

Ms. DEGETTE. Thank you. And just to reiterate, several of the members expressed to me during the votes that they will submit their questions in writing, so if we can get responses to all these questions, it would be great.

Dr. COLLINS. We are happy to do that.

Ms. DEGETTE. And I want to remind all of the members that they may submit additional questions for the record to be answered by the witness. The questions should be submitted to the clerk within 10 days and then the clerk will notify all of the offices of the procedures.

And I would like to just thank you in particular, Dr. Collins. You have a very full plate. We are glad you gave us your afternoon. It was a wide range of questions. The members, I think, were impressed by the answers and we look forward to working with you, and this meeting is adjourned.

[Whereupon, at 4:30 p.m., the Subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Statement of Congressman Gene Green
Committee on Energy and Commerce
Subcommittee on Health
NIH in the 21st Century
June 15, 2010

Mr. Chairman, thank you for holding this hearing today on the NIH.

The NIH, the world's leading biomedical research institution, is one of the great success stories of the federal government. Our investment in this life-saving research has led to advances that have profoundly improved the length and quality of life for millions of Americans.

Information gained from NIH research is revolutionizing the practice of medicine and future directions of scientific inquiry.

Without a doubt, the work performed at the NIH is invaluable. The groundbreaking research supported by NIH has provided a lifeline of hope to countless Americans living with diabetes, cancer, HIV/AIDS and many other illnesses.

I was proud to support the NIH because my hometown of Houston is home to the world-class Texas Medical Center, which houses many facilities that conduct groundbreaking NIH research.

The Baylor College of Medicine and Texas Children's Hospital conduct more NIH pediatric research than any other NIH grantee.

The University of Texas's MD Anderson Cancer Center also conducts critical NIH research and is frequently recognized as the top cancer center in the country.

I believe it is crucial that the NIH be appropriated adequate funding level by Congress so that NIH research performed at the Texas Medical Center – and other impressive research facilities across the nation – will yield continued contributions to our understanding of disease and the development of effective treatments to improve the health and well-being of all Americans.

With the passage of the American Recovery and Reinvestment Act (ARRA), the NIH was awarded $10.4 billion dollars to fund and support biomedical research. To date, the NIH has awarded 12,000 grants in nearly 166 different topics in biomedical research.

Millions of dollars in ARRA NIH grants have been awarded to UT, Baylor, MD Anderson, and many other Texas medical research institutions. These investments have not only created many biomedical jobs, but also furthered our investment in medical research.

I believe it is crucial that we continue to fund the NIH at a level in which they can continue to award grants throughout our country so that research performed at the Texas Medical Center – and other impressive research facilities across the nation – will yield continued contributions to our understanding of disease and the development of effective treatments to improve the health and well-being of all Americans.

I want to thank Dr. Collins for appearing before the Committee today. I look forward to hearing an update on current research and activities at the NIH.

Thank you Mr. Chairman, I yield back my time.

The Honorable Joe Barton
Committee on Energy and Commerce
Subcommittee on Health
NIH in the 21st Century: The Director's Perspective
June 15, 2010

Thank you Mr. Chairman for holding this hearing, and thank you Dr. Collins for being here to testify.

When I became Chairman in 2004, I made it my priority to get something done that no one had been able to do since 1993 – reauthorize the National Institutes of Health. Congress had doubled the agency's budget, but we never managed to follow through on our obligation to ensure the agency was modernized to introduce effective, contemporary management of medical and scientific research. With the help of stakeholders, Director Elias Zerhouni, Chairman Dingell, and all the other Members of

the Committee, we did what many said could not be done and reauthorized the NIH.

I think that process showed what this Committee can do when it works together. We did not replace meritorious scientific priorities with political talking points. The NIH Reform Act was about providing the NIH the management tools to do medical research in the 21st Century and the mechanisms of transparency so Congress and the public could be confident about the work of the NIH.

One of the most important tools was the creation of the Common Fund. Since its inception, the National Institutes of Health have been essentially a conglomeration of different and essentially separate organizations. Each disease or specialty was

dealt with within a semi-autonomous research silo. As scientific knowledge has improved and research has advanced, it has become apparent that the silos mostly served those who worked inside them, and in doing so they acted as fortresses against the dispersal of vital medical information. It was as if the NIH management organization had been intentionally created so that the left hand would never know what the right hand was doing, and visa versa.

The NIH is now compromised of 27 different Institutes and centers, yet the causes and effects of diseases like Parkinson's reach across the scope of numerous Institutes. The Common Fund attempts to break down the walls between these Centers by serving as a source of funding for collaborative research. That's

why I am excited to hear from Dr. Collins about how well the Common Fund is doing its job.

Last year, Congress appropriated a one-time lump sum of $10.4 billion to the NIH and called it economic stimulus. I strongly support fully funding the NIH, but thought that it was deeply disingenuous of the Obama administration to pretend that spending at NIH was going to reverse the recession. My opinions have not changed. Each year, every lawmaker in this Congress is visited by numerous impassioned, well-intentioned groups asking for more funding for at NIH for their particular cause. We do them no favor by saying yes. Instead, it must be our responsibility to ensure that whatever resources we provide

to the NIH are spent in the name of good science instead of good politics.

That the Stimulus bill was more about politics than science was evident in the fact that it directed the NIH to spend like a house afire. It was to jettison its stimulus funding within two years and, in doing so, it was to ignore the fact that meaningful science requires the kinds of planning that is controlled by the facts instead of the calendar. Studies need to be designed, sample groups selected, and experiments performed and repeated. That's why most NIH grants are for four or five years. Throwing money out the door to satisfy a political agenda turns methodical scientific method into gambling, and it does not even create the desired economic growth.

I appreciate the Chairman holding this hearing. It is important for this Committee to conduct its oversight responsibilities of the NIH. I remain disappointed, however, that we continue to fail to hold hearings on the new health care law. We have already seen numerous failures in that implementation. The Government mailed postcards to 4 million small businesses alerting them of a tax credit for which only a small fraction are eligible. We have seen the Department of Health and Human Services mail Medicare brochures that were false and misleading. And yesterday, the Administration released draft regulations showing that 51 percent of Americans with employer-sponsored health care will see their benefits change. The President and certain Members of this Committee promised Americans that if they liked what they had they could keep it. That promise is being broken. This Committee has a

responsibility to hold hearings on the implementation of the law, and Members who voted for the legislation should demand it to ensure that their promises to the American people are not broken.

With that Mr. Chairman, I look forward to hearing Dr. Collins' testimony and hearing his suggestions for how this Committee can move forward to reauthorize this important agency. I yield back my time.

Congress of the United States
Washington, DC 20510

June 14, 2010

Dr. John Niederhuber
Director, National Cancer Institute
Building 31 - Claude D Pepper Building, 11A48
31 Center Drive
Bethesda, MD 20814

Dear Dr. Niederhuber,

We write to express our strong support for an increased federal investment by the National Cancer Institute (NCI) to find a cure for gastric cancer.

The need for a timely and sustained investment in research on this disease is clear. As you know, gastric cancer is one of the deadliest cancers in the U.S. In 2009, there were an estimated 10,620 deaths from gastric cancer. The five-year survival rate for metastatic gastric cancer is 3.4 percent, one of the five lowest cancer survival rates.

Just last month, NCI released a study revealing a dramatic increase in gastric cancer in young people. For Americans age 25-39, the likelihood of being diagnosed with gastric cancer has increased by almost 70 percent since 1977.

The revelation of this alarming increase is particularly grim because the prognosis for younger adults diagnosed with gastrointestinal (GI) cancers is very poor. Because of the lack of symptoms, the disease is usually in late stage by the time the diagnosis is established. As a result, GI cancers in young people have very low survival rates. Unfortunately, current research, both federally and privately funded, is not keeping pace with this deadly disease.

Scientific understanding of this disease and the development of treatment options will only improve if investments in research are made. We commend you for your efforts to date and would like to work with you to further research on gastric cancer.

In the House and Senate Appropriations Committee Reports for Fiscal Year 2010, Congress asked NCI to increase its attention to gastric and other gastrointestinal cancers and to consider developing a biorepository to expedite potential treatment for late stage cancer. The need for additional research on gastric and other deadly cancers was also a focus of a March congressional hearing on cancer in the House.

We understand that gastric cancer is one of the cancers selected to be part of The Cancer Genome Atlas (TCGA). We urge you to make the collection and analysis of high quality biospecimens a priority. In anticipation of the monumental data that will come from this project, we ask NCI to convene a workshop of experts in the field of gastric cancer to develop a plan to stimulate research by the very best investigators and cancer centers in the U.S. We also expect

NCI to develop a research agenda and issue a specific Request for Proposals (RFA) on gastric cancer.

These steps—analysis of gastric cancer by TCGA, an expert workshop to strategize how to solve this problem and an RFA to stimulate research by the very best in the field—could make a dramatic impact on the understanding of gastric cancer; potentially providing the data to develop screening mechanisms, treatments and cures.

It is essential that NCI take these steps to ensure the critical advancement of efforts to understand and cure this deadly disease, and we offer our committed support to assist in this effort.

Sincerely,

Richard J. Durbin
United States Senator

John Shimkus
Member of Congress

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

AUG 2 0 2010

The Honorable Henry A. Waxman
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

This is in response to your June 30 letter transmitting questions for the record following the June 15 Subcommittee on Health hearing entitled "NIH in the 21st Century: The Director's Perspective." I enjoyed appearing before the Subcommittee and am pleased to provide additional information. Enclosed please find responses to the questions submitted.

Sincerely yours,

Francis S. Collins, M.D., Ph.D.
Director

Enclosure

The Honorable Bart Gordon

1. **As you know, I am a firm believer in the outcomes-oriented research strategy so successfully employed by the Advanced Research Project Agency at DOD. For that reason, I have championed ARPA-E, a program of high-risk, high-reward research at the Department of Energy. Alzheimer's is a looming public health challenge of enormous scale that threatens the solvency of Medicare and Medicaid, particularly given the aging of the Baby Boom generation.**

   Would it be useful to use the ARPA-E model to create an outcomes-oriented program of research specifically targeted at critical public health threats like Alzheimer's at NIH?

Flexible funding and hiring authorities can be useful tools for agencies to address challenges such as the ones described above. The ARPA model may be worthy of replication at other agencies, as you have made possible at the Department of Energy. In fact, Congress has already provided NIH with some flexible funding authorities. The Cures Acceleration Network (CAN), authorized through the Affordable Care Act, is an example.

CAN is expected to provide an integrated and very rapidly moving ARPA-like effort to stimulate therapeutic development in areas of high need. While we have a number of programs already under way to advance the translational medicine pipeline, CAN would give us greater flexibility to pursue promising therapeutic targets. In addition to supporting the development of novel molecules and efforts to repurpose abandoned products, it would provide NIH with an unprecedented opportunity to re-engineer the therapeutic development pipeline by smoothing the pathway for developing new drugs, biologics, and devices, particularly through the "valley of death" phase of the pipeline where an extremely high failure rate is drying up private investment. The CAN authorization includes a new process that would take advantage of powerful new technologies and involve close coordination with the Food and Drug Administration (FDA) and strong partnerships with private sector stakeholders working in a transparent and collaborative environment. The CAN authorities would allow NIH to coordinate NIH-funded research with FDA approval requirements, leverage private and non-profit sector resources through a 1:3 matching program, and enable the NIH Director to fund and, when necessary, de-fund projects quickly.

The NIH also has flexible research authorities through the NIH Common Fund, which was enacted into law by Congress through the NIH Reform Act to support cross-cutting, trans-NIH programs. The Common Fund is supporting the development of novel therapeutic approaches to a number of conditions through high risk, outcome-driven research projects.

Other funding mechanisms also enable us to support high risk-high reward research. These include the NIH Director's Pioneer, Exceptional, Unconventional Research Enabling Knowledge Acceleration (EUREKA), and New Innovator Awards. One of the recipients of a EUREKA

program award is conducting research on the role of amyloid precursor protein (APP) signaling in Alzheimer's disease at the University of California, San Francisco.

The Honorable Gene Green

1. **Earlier this year, the House passed a resolution I authored to recognize the need for type 1 diabetes research funding and the importance of the Special Diabetes Program at the NIH.**

   This program is funding important research across all stages of the disease, including the complications of diabetes. As the founder of the Congressional Vision Caucus, I know that diabetic eye disease is the leading cause of blindness in working age adults.

   As such, research in this area will have tremendous implications for society. I read recently that researchers have found a way to not only halt the progression of diabetic eye disease but reverse the disease in patients enrolled in clinical trials supported by the Special Diabetes Program.

   Can you please comment on this research and what you see for the future for those affected by this complication of diabetes?

Diabetic retinopathy is a leading cause of blindness in the U.S. and a major complication of diabetes. Fluid leaking from newly formed, but abnormal, blood vessels in the eye leads to retinal swelling and vision loss. For the past 25 years, diabetic retinopathy has been treated with a laser to destroy abnormal blood vessels. Although laser therapy slows disease progression, the effects are temporary, and repeated treatments can damage healthy retinal tissue and impair vision.

A major factor contributing to abnormal blood vessel growth in diabetic retinopathy is the secretion of a protein, vascular endothelial growth factor (VEGF). Blocking secretion of VEGF in the eyes of diabetic patients could lead to stabilization or improvement of vision. A recent clinical trial compared the effectiveness of the current standard laser therapy with a new treatment regimen where laser therapy was combined with Lucentis, a drug that inhibits VEGF. The combination therapy was found to be superior to standard laser therapy alone. Nearly 50 percent of patients who received the combination treatment experienced significant visual improvement after one year compared to 28 percent who only received laser treatment. Vision continued to decline in very few patients treated with the combination therapy (less than 5 percent) compared with almost 15 percent who received standard laser treatment alone.

Lucentis is FDA-approved for another blinding disease attributed to VEGF release, age-related macular degeneration, so clinicians already are using Lucentis to treat diabetic retinopathy. This clinical advance should lead to a dramatic improvement in the visual health, independence, and quality of life of patients with either type 1 or type 2 diabetes.

The trial, cofunded by the National Eye Institute and the Special Funding Program for Type 1 Diabetes Research, was conducted by the Diabetic Retinopathy Clinical Research Network, a nationwide network spanning 37 States and including 102 community-based clinics and

academic centers, comprising about one-third of U.S. retina specialists (http://drcrnet.jaeb.org/ViewPage.aspx?PageName=Home).

2. **As you know Chronic Obstructive Pulmonary Disease (COPD) is the 4th leading cause of death in the United States, and the only one of the top 5 causes of death that is currently on the rise.**

   The National Heart, Lung, and Blood Institute recently started the Learn More Breathe Better Campaign to raise public awareness of symptoms and treatment options for COPD. What additional steps do you envision NIH taking to address COPD?

The National Heart, Lung, and Blood Institute (NHLBI) supports research that addresses a broad spectrum of scientific needs and opportunities related to COPD. Significant progress is being made on four key fronts— therapeutic trials, personalized medicine, pathological mechanisms, and research dissemination.

Large, multicenter clinical trials supported by the NHLBI are evaluating the efficacy of several currently available therapies. For example, the Long-term Oxygen Treatment Trial is testing the ability of supplemental oxygen treatment to prevent deaths and hospitalizations in patients with COPD and less-than-severe hypoxemia. Other trials in the Institute's COPD Clinical Research Network are testing whether azithromycin or simvastatin, drugs approved for other purposes, can be used to reduce the frequency of COPD exacerbations. A new NHLBI program, Centers for Advanced Diagnostics and Experimental Therapeutics in Lung Diseases (CADET), is being established to accelerate the development of agents for the diagnosis and treatment of lung diseases such as COPD based on an understanding of the underlying pathological processes of disease.

Because COPD involves a wide range of abnormalities, appropriate treatment may vary from one patient to another. Studies are under way to identify subgroups of patients for whom different therapeutic approaches should be used. The COPDGene study will evaluate 10,000 current and former smokers, with and without COPD, to categorize the various abnormalities seen on x-ray CT lung images and identify genetic traits associated with specific disease manifestations. The Lung Genomic Research Consortium, supported through the American Recovery and Reinvestment Act of 2009, is performing state-of-the-art, high-throughput molecular analyses of lung tissues from patients with COPD to find molecular "fingerprints" that indicate different disease subtypes. The "SubPopulations and InteRmediate Outcome Measures In COPD Study" (SPIROMICS) will characterize subpopulations of COPD patients by using extensive molecular and clinical measures and also identify intermediate outcome measures that may be useful in future clinical trials.

Although substantial improvements in patient care and outcomes may be possible through better use of existing treatments, prevention or cure of COPD will likely require innovative treatments that address specific disease mechanisms. The NHLBI supports a number of investigator-initiated projects on disease pathogenesis and is currently renewing its Lung Tissue Research

Consortium, which collects lung specimens and distributes them for use in COPD research. In addition, the NHLBI and the NCI have recently joined to promote research on cellular and molecular mechanisms that contribute to both COPD and lung cancer, closely related diseases that together cause over a quarter of a million deaths in the U.S. each year.

The Learn More Breathe Better campaign is being expanded to involve State and local partner organizations in COPD awareness activities. Recognizing that disease surveillance is essential for formulation of an effective public health program, the NHLBI will be funding a module on COPD in the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System survey beginning in 2011. The availability of State-specific COPD data will inform regional efforts to control COPD and document its burden throughout the Nation.

3. **I have a personal interest in Tuberculosis research at the NIH.**

   People often view TB as a disease that threatens third world populations, but TB has been resurging in the US.

   Over the past couple of years there have been several TB scares in the US and in my district.

   I was the sponsor of the Comprehensive TB Elimination Act (HR 1532), which became law in 2008. This legislation aims to eliminate TB domestically and would intensify efforts to prevent, detect, and treat individuals in our country with TB.

   Can you tell me what type of research the NIH is conducting with regard to TB? I know the NIH has been working on a TB vaccine. What is the status of that research?

The National Institute of Allergy and Infectious Diseases (NIAID), through grants and other mechanisms and in its intramural research program, supports a globally relevant tuberculosis (TB) research agenda. NIAID's TB research encompasses all aspects of TB, including drug-sensitive and drug-resistant TB, as well as TB in HIV-infected persons. NIAID-sponsored basic TB research seeks to better understand the biology of TB and the host-pathogen interaction, including latent TB infection in human hosts and in animal models of infection and disease. NIAID-supported translational and clinical research focuses on the identification and development of new diagnostics, drugs, and vaccines. To understand TB in special populations, NIAID's research agenda includes efforts to study TB in children and immune-suppressed persons and to clarify the interaction of HIV and TB to improve TB prevention and treatment in adults and pediatric populations. NIAID's investments in basic, translational, and clinical science have led to the development of several new candidate TB drugs, diagnostics, and vaccines.

Specific NIAID research activities include the following:

- In fiscal year (FY) 2008, NIAID published the NIAID Research Agenda for Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis (MDR/XDR-TB). This agenda complements and leverages ongoing NIAID TB research efforts and focuses on specific research gaps related to MDR/XDR-TB.

- In FY 2008, NIAID awarded grants to study the pharmacological basis of drug resistance in infectious diseases; several TB grants are supported under this mechanism.

- NIAID is supporting studies to characterize drug-resistant TB strains, their epidemiology, and their impact on disease progression, host immune response, and response to therapy.

- In FY 2009, NIAID established a Clinical Diagnostic Research Consortium (CDRC) to provide expertise for the evaluation of early stage diagnostic candidates, including diagnostics for TB.

- In FY 2010, NIAID began support of targeted clinical trials to evaluate and improve the optimal use of currently existing therapies for TB. NIAID also is currently supporting Phase I clinical studies of new TB drug candidates.

- NIAID currently is exploring collaborative activities with the Institute's extensive HIV/AIDS clinical trials networks to increase research on drug-sensitive and drug-resistant TB as a co-infection in patients with HIV/AIDS. This collaboration will significantly increase the capacity for international clinical trials on TB and will increase support to combat the co-epidemics of TB and HIV.

- On July 29-30, 2010, NIH hosted a Forum with several key partners including FDA and CDC to promote TRIUMPH: TB Research in Underserved Maternal and Pediatric Populations with HIV. The purpose of the meeting was to discuss approaches to develop diagnostics and therapies for women and children co-infected with HIV and TB.

- NIAID's intramural research program has an active TB research portfolio. In 2009, researchers at NIAID, in collaboration with NIAID grantees, published a paper in *Science* magazine showing that a combination of metronidazole and linezolid, two commonly used and FDA-approved antibiotics, could kill extensively drug-resistant TB in the laboratory. NIAID researchers are currently collaborating with drug manufacturers and international colleagues at the Masan National Tuberculosis Hospital in South Korea to launch a clinical trial of the drug combination in individuals who have multidrug-resistant TB (MDR-TB) or extensively drug-resistant TB (XDR-TB). The Masan Hospital has the largest population of inpatients with MDR-TB in the world. In addition to this trial, the researchers are characterizing the genetic changes in MDR-TB and XDR-TB bacteria that make them unique beyond their mutations in drug-resistance genes. Investigations to develop new point-of-care diagnostic tests are assessing the presence of TB in easily

accessible human samples, such as urine and exhaled breath condensate. Efforts are also under way to detect TB drug-resistance genes in sputum samples so that effective drug treatment can be prescribed at the initiation of therapy.

- In 2009, NIAID signed an Implementation Arrangement with the Henan Provincial Health Bureau to begin studies on highly drug-resistant TB in Zheng Zhou, the capital city of Henan province in central China. Henan province has the highest number of drug-resistant TB cases in the world. NIAID has provided training in the conduct of clinical trials to scientists and physicians from Zheng Zhou and has worked with the province to prepare for the studies. Patient enrollment in the first clinical trial undertaken under this agreement began in March 2010.

- NIAID drug-sensitive and drug-resistant TB research activities are coordinated with other Federal agencies through the U.S. TB Task Force, as well as with other government and non-governmental organizations such as the World Health Organization/Stop TB Partnership, programs funded by the Bill & Melinda Gates Foundation, and not-for-profit product development partnerships.

Vaccines

The development of a safe and effective TB vaccine is a top NIAID priority. Current TB control strategies are limited and focus on identification of patients with symptoms of pulmonary TB and treatment with combination antibiotic therapy. The search for a newer, more effective TB vaccine is made more urgent as some TB patients, including those co-infected with HIV/AIDS, may not display classic symptoms of pulmonary TB and therefore may not be detected with current strategies. The current vaccine, Bacille Calmette-Guerin (BCG), provides protection against TB complications in infants and young children but does not substantially lower the burden of transmissible, pulmonary TB in adults.

NIAID supports research to identify new candidate TB vaccines. Candidates are targeted to boost pediatric BCG vaccination or to eventually replace BCG with longer lasting, more effective vaccines. Candidate classes being developed include virally vectored, adjuvanted subunit, and live and live-attenuated vaccines. NIAID also supports research on the use of immune-boosting strategies to prevent infection or disease and to evaluate the potential of synthetic vaccines to shorten TB drug treatment regimens.

In addition, NIAID funds vaccine development, including preclinical animal studies and clinical research, on the most promising candidate TB vaccines. Several vaccine candidates that demonstrated protection against infection with TB in small animal models have entered human clinical trials.

The greatest challenge in TB vaccine development is to understand how TB evades the host immune system, since natural infection with TB does not always protect against subsequent infection and disease. NIAID is supporting immune studies in humans and animals to determine the properties necessary for new vaccine candidates.

The Honorable Diana DeGette

Pediatric Research Consortia Questions

1. **As the leader of the team that successfully mapped the human genome, you know more than almost anyone about how this knowledge has transformed biomedical research. Thanks to the work you led, the earliest studies to take advantage of the genome project suggest the relationship between health and disease begins before birth and during early infancy, with significant consequences showing up in childhood and into adulthood. Given these findings, I have introduced the Pediatric Research Consortia Establishment Act—legislation modeled upon similarly successful NIH endeavors and focused on enhancing pediatric biomedical research.**

   At its core, the proposal envisions a networked consortium of leading pediatric biomedical research entities that would be competitively selected by NIH. A networked hub-and-spoke model would foster resource sharing and collaboration among small and large institutions to ultimately generate a stronger return on investment and help us develop treatments and therapies for diseases and disorders of both childhood and adulthood. What are your thoughts on such a networked hub-and-spoke style approach, particularly in the pediatric arena?

In FY 2009, 22 Institutes and Centers (ICs) of the National Institutes of Health (NIH) awarded approximately $3.4 billion, including funds from the American Recovery and Reinvestment Act, for pediatric research activities across the country. This funding was distributed to the research community through the full range of available funding mechanisms, including investigator-initiated grants, contracts, and research networks. This flexibility allows the extensive scientific expertise at NIH and across the extramural scientific research community to judge which mechanism(s) might best be suited for the specific research needed to answer questions about children's health and development, diseases, and conditions. Less commonly, but where the scientific challenge warrants and funding permits, NIH ICs (often in trans-Institute collaboration) have created multidisciplinary centers of excellence or research networks for specific pediatric populations or conditions, such as autism, pediatric oncology, neonatology, and adolescents with HIV/AIDS, to name a few.

In addition, a number of the Clinical and Translational Science Awards (CTSAs) sites include a strong emphasis on creating infrastructure to conduct pediatric clinical trials, which will allow pediatric researchers who focus on a wide variety of conditions to utilize this new resource and to conduct clinical trials efficiently and effectively.

The NIH may not comment on pending legislation on which the Administration has not yet taken a position. However, in evaluating what mechanism or infrastructure to use to address any question about health or disease, important considerations include whether the proposed mechanism provides the range of scientific expertise required to answer that question, the availability of a sufficiently sized study population, and whether a currently existing mechanism

might adequately meet these needs. The impact of creating a new infrastructure on investigator-initiated proposals also must be weighed.

2. **Pediatric research has historically faced a number of challenges, both within NIH and beyond. For example, the fact that most diseases of childhood are rare diseases often makes it extremely difficult, if not impossible, to conduct trials in one geographic area simply because of a lack of participants. This and other barriers are problematic not only for our nation's children, but also for adults because we know a number of conditions may be rooted in the pediatric years even if they do not manifest until adulthood. How do you think NIH can overcome these challenges and make the necessary commitment to pediatric biomedical research needed for the 21st Century?**

A rare disease is one that affects fewer than 200,000 individuals in the U.S. Yet, taken together, over 6,000 rare diseases afflict more than 25 million people in the U.S., including children. Since private pharmaceutical companies are developing relatively few therapeutics for these diseases, the NIH is sponsoring various programs to bridge the gap between basic research and human testing of new drugs. The Therapeutics for Rare and Neglected Diseases (TRND) program is a collaborative drug discovery and development program that will enable certain promising compounds to be taken through the preclinical development phase. Compounds that prove successful in these early, high-risk trials can then be turned over to private companies for further testing through cooperative agreements. Although this new program, which received $24 million in FY 2009, is not focused solely on the pediatric population, some of the compounds that it is studying will benefit children.

In addition, the NIH Office of Rare Diseases was directed by Congress in the Rare Diseases Act of 2002 (P.L.107-280) to establish a clinical research network focusing on rare and neglected conditions. Since 2003, the Rare Disease Collaborative Research Centers network of investigators and patient groups, in partnership with technology leaders, has been working to develop biomarkers and new approaches to diagnosis, prevention, and treatment; provide content for a Web-based resource site about rare diseases; and train new clinical investigators in rare disease research. Currently, of ten member sites of the network, two are focused on pediatric rare diseases. These two main sites and their 13 affiliate sites (many located at children's hospitals) are managed by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) on behalf of the NIH.

The Rare Disease Collaborative Research Centers network is only one of nearly 60 networks of researchers in which the NICHD has a leadership role, the majority of which focus on various aspects of children's health and development or pediatric conditions. Others include the Adolescent Medicine Trials Network for HIV/AIDS Interventions, the Collaborative Pediatric Critical Care Network, the Global Network for Women's and Children's Health Research, and the Neonatal Research Network. Each of these takes advantage of scientific expertise that may be widely dispersed across the country, or even around the world, and the use of common protocols to maximize research potential, even with small populations in any one location.

Precursors to adult disease can occur even earlier than birth, yet may not manifest themselves until later in life, making it difficult to study retrospectively what the causes of disease may have been, or conversely, what early activities or preventive measures may lead to a healthier adulthood.

The Honorable John P. Sarbanes

1. **The Institute of Medicine recently released a report, A National Cancer Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program, which highlights many troubling aspects about the National Cancer Institute's clinical trial program. The report notes, "the program is falling short of its potential to conduct the timely, large-scale, innovative clinical trials needed to improve patient care" and found that many of these shortcomings are due to an inefficient, cumbersome, underfunded and overly complex system. The report makes four key recommendations that are needed to improve those efforts.**

    a. **What concrete steps are you taking to implement these recommendations and to improve the program in a timely manner?**

    b. **What will the new NCI director's role be in implementing these recommendations?**

    c. **Please provide a timeline for implementation and next steps.**

a. What concrete steps are you taking to implement these recommendations and to improve the program in a timely manner?

It is important to make clear that the National Cancer Institute (NCI) commissioned the Institute of Medicine (IOM) report to gather independent and expert perspectives on the state of cancer clinical trials and to obtain advice about improvements in the NCI Cooperative Group Program. We believe it is important to re-evaluate our flagship programs periodically to ensure that they function optimally. It is, however, noteworthy that over the past 5 years, more than 17 Cooperative Group trials have significantly affected how oncology is practiced currently in the United States. In addition, while the IOM review was under way during the past year, NCI was simultaneously implementing many of the ideas that were recommended in the final IOM report. For example:

- **Increasing Reimbursement to Sites:** NCI has recently increased the per case reimbursement rates from $2,000 to $5,000 *for phase 2 studies*, and additional funding beyond the standard $2,000 for *selected phase 3 trials* based on their complexity.

- **Setting Deadlines for trial development:** Data has shown that a trial that does not open to accrual within two years of concept submission is very unlikely to reach full accrual. After that length of time, the scientific questions have often evolved, and there are typically more scientifically relevant studies being proposed. Based on this analysis, NCI instituted new deadlines, which will take effect January 1, 2011, enacting the

recommendations of the Operational Efficiency Working Group (OEWG),[1] to halve the time it takes to start new clinical studies and terminate studies not activated within two years of concept approval. As of April 15, 2010, all new studies are undergoing a revised approval and implementation process that targets going from the initial idea to a complete study in 7 and 10 months for phase 2 and 3 trials, respectively.

- **Funding dedicated staff positions for rapid trial development:** To aid the more rapid implementation of trials, the American Recovery and Reinvestment Act has provided the opportunity for NCI to fund dedicated staff positions – within NCI and at the cooperative groups – with expertise such as science writing and clinical trials management – to keep trials on schedule for development and meeting deadlines. Goals are: (1) trial development steps that occur in parallel; (2) direct, coordinated interactions to resolve issues; and (3) continuous use of protocol tracking tools and overall project management.

- **Prioritizing the most important trials:** NCI has revamped the process for prioritizing the large phase 2 and 3 cancer treatment and control trials. In place of the prior NCI-only review, the Institute has established disease-specific and modality-specific (imaging and cancer control) Steering Committees comprising expert investigators from the Cooperative Groups and Cancer Centers along with patient advocates to prioritize the best ideas for these large-scale trials. Once approved by these Steering Committees, NCI staff works with the lead investigators to facilitate rapid development of the final study, coordinating with other key stakeholders such as pharmaceutical collaborators and the FDA as necessary.

- **Encouraging Common Business Practices Across Cooperative Groups:** NCI has already achieved a good deal of integration by forming the Cancer Trials Support Unit (CTSU) – a program started around 2000 but greatly expanded over time and continually being improved - that provides the Groups' operations offices, the investigator sites, and the patients with a one-stop shop for protocol-related materials and information. The CTSU provides a single repository for all regulatory documents across all Group trials and offers a 24-7 online registration system for all Group trials. Most importantly, it allows investigators, irrespective of their Group membership, to enroll their patients in any suitable trial on the CTSU listing. This has permitted over 40 percent of enrollments to Group trials to come from sites that are not a member of the Group leading the trial. NCI has invested in standardizing case report forms, defining data elements, and bringing uniform database capabilities to all the groups.

[1] The NCI Clinical Trials and Translational Research Advisory Committee (CTAC) established the Operational Efficiency Working Group to recommend strategies for reducing the time for activation of Cooperative Group and Cancer Center trials. The 68-member group includes leadership from the Groups, Cancer Centers, and community oncologists, as well as representatives from the Food and Drug Administration, the Centers for Medicare and Medicaid Services, and NCI.

- **Modernized Clinical Trials IT Infrastructure:** NCI is in the process of procuring a single information system (clinical trials data management system) for the entire NCI clinical research enterprise. This will be made available to the Groups in 2010 and will facilitate a series of new innovations including:
    - standardized case report forms
    - a common protocol authoring tool
    - consistent audit standards
    - enhanced data sharing

- **Improving Efficiency and Utilization of NCI Centralized IRB:** NCI has been working to increase utilization of the NCI Centralized Institutional Review Board (IRB), improve efficiency overall, and decrease the average time for final sign-off on a national protocol from 150 days in 2007, to 36 days in 2009-2010. NCI is also in the process of obtaining national accreditation for the Centralized IRB, which should be a significant boost to increased participation. Approximately 700 cooperative group sites (out of 1800) are already participating in the Centralized IRB, and more than half of the Comprehensive Cancer Centers have joined the Centralized IRB.

b. What will the new NCI director's role be in implementing these recommendations?

NCI staff has fully briefed Dr. Harold Varmus, the new NCI Director, about the NCI Clinical Trials Enterprise, including the recommendations of the IOM and the OEWG about ways to improve clinical trials. This is a high-priority issue for NCI, and plans for continued improvements to the NCI clinical trials system will receive full attention from Dr. Varmus.

c. Please provide a timeline for implementation and next steps.

NCI has already made or is in the process of implementing several major changes to the clinical trials system, such as instituting trial development deadlines, increasing reimbursement to the sites, and funding dedicated staff positions for protocol development. Implementation of a state-of-the-art clinical trials data management system across all Cooperative Groups and many Cancer Centers will reduce training costs for research nurses and clinical research associates. It will enhance the ability to share clinical data across trials allowing for meta-analyses and more comparability studies. And, perhaps most importantly, it will enable more consistent data standards to be applied in all NCI-sponsored Cooperative Group trials, allowing for improved patient safety and timely reporting of trial outcomes. Full-scale integration of modernized clinical trial IT infrastructure is an ongoing effort, with implementation efforts set to begin in selected Cooperative Groups this year and all Groups coming on board with the new system by 2011.

The Honorable Zack Space

Congenital Heart Defects

1. **While the toll of diabetes and some other chronic diseases has been well-documented, NIH must also focus attention on new chronic diseases that exist due to successes in science and health care during the late 20th century, such as congenital heart disease. Successes in medical interventions in children with congenital heart disease have led to a new chronic population that will need specialized care throughout their lives.**

   As you are aware, the Patient Protection and Affordable Care Act included provisions from a bill I introduced last year, the Congenital Heart Futures Act. In the health reform law, section 10411 notes that NIH may expand, intensify, and coordinate research and related activities with respect to congenital heart disease, including research with respect to the causation of congenital heart disease, including genetic causes, long-term outcomes in individuals with congenital heart disease, and that NIH may help to identify barriers to life-long care for individuals with congenital heart disease.

   Can you discuss NIH's planned activities to ensure a proper focus on congenital heart disease - from prevention to life-long treatment - given what an important 21st century chronic disease it is?

Despite significantly improved survival and advances in surgical technique, there are no "cures" for many forms of congenital heart disease (CHD). Identifying causes, improving treatments, and understanding what drives long-term outcomes for patients with CHD are all important factors for addressing this chronic disease.

The human heart is the first organ to be formed in embryonic life, growing from a few cells to a fully functional four-chambered circulatory pump in just under 10 weeks. Understanding the genetic underpinning of this astonishing developmental feat is the goal of the recently launched Cardiovascular Development Consortium (part of the Bench to Bassinet Program launched earlier this year by the National Heart, Lung, and Blood Institute (NHLBI)). Scientists across the United States will participate in an unprecedented collaboration to identify the complex network of molecular and genetic signals that lead to the formation of normal and abnormal hearts. Another partner in the Bench to Bassinet program, the Pediatric Cardiac Genomics Consortium, will study individuals of all ages with CHD to determine its genetic causes and the genetic factors that affect long-term outcomes.

Much of the improvement in CHD survival is a result of surgical advances. The third component of the Bench to Bassinet Program, the Pediatric Heart Network (PHN), recently completed a landmark randomized trial in babies with complex CHD. Aided by strong collaboration between congenital heart surgeons and pediatric cardiologists, the PHN enrolled 555 newborns over a 3-year period and evaluated surgical strategies to correct the heart defect. The wealth of data

collected about the clinical course during the first year of life of these fragile infants will continue to be analyzed intensively, helping us to identify risk factors for short- and longer-term outcomes. Another important treatment initiative is the PumpKIN (Pumps for Kids, Infants, and Neonates) Program, which is developing cutting-edge circulatory support systems for infants and children. PumpKIN is moving bench-top testing previously funded by the NHLBI to testing in children over the next 3 years. When the devices are ready for testing, they can be evaluated through the PHN. The NHLBI's Children and Clinical Studies Web site (http://www.nhlbi.nih.gov/childrenandclinicalstudies/index.php) provides an accessible resource for families about what to expect when participating in clinical research, which greatly facilitates recruitment.

Recognizing the importance of CHD as a chronic condition, one of the PHN's studies enrolled children 6-18 years of age with complex heart disease and is following them over time with the aim of identifying barriers for their transition to appropriate adulthood care and services. In addition, NHLBI is planning to fund a novel grant that will use an electronic health record designed for adults with CHD to identify pressing research needs in this population and engage affected individuals in the research. The NHLBI is an active partner in the Congenital Heart Disease Public Health Consortium, led by the Centers for Disease Control and Prevention; one of the goals is to develop a registry so that individuals born with CHD can be followed throughout life.

○